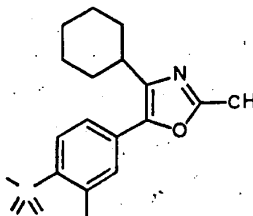


-318-

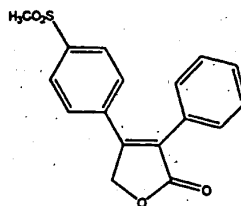
1)



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-319-

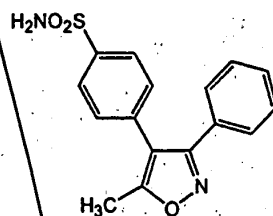
5)



rofecoxib, 4-(4-(methylsulfonyl)phenyl)-3-phenyl-2 (5H)-furanone,

5

6)



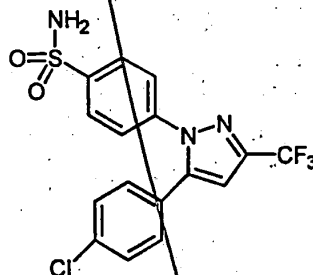
4-(5-methyl-3-phenylisoxazol-4-yl)benzenesulfonamide,

7)

N-[[4-(5-methyl-3-phenylisoxazol-4-yl)phenyl]sulfonyl]propanamide,

10

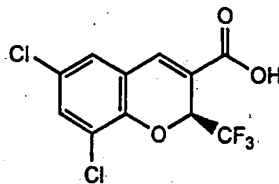
8)



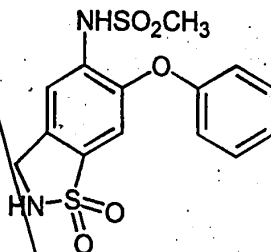
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazole-1-yl]benzenesulfonamide,

-320-

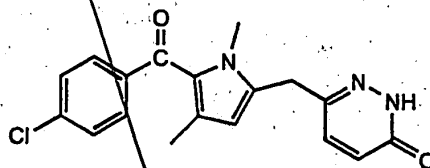
9)



10)

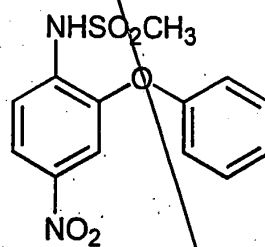


11)



6-[[5-(4-chlorobenzoyl)-1,4-dimethyl-1H-pyrrol-2-yl]methyl]-3(2H)-pyridazinone,

12)



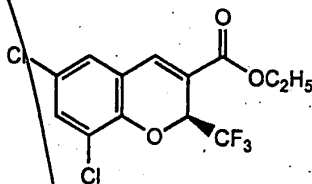
N-(4-nitro-2-phenoxyphenyl)methanesulfonamide,

10

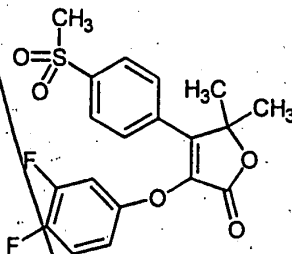
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T05001.290898

-321-

13)



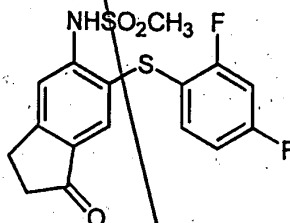
14)



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3-(3,4-difluorophenoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-2(5H)-furanone,

15)

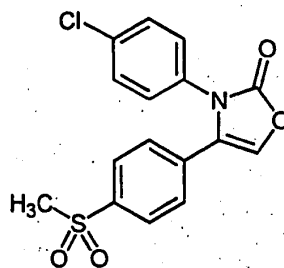


N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,

10

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10880063-100501
TOS:00/37107

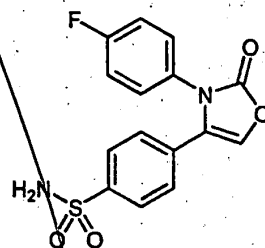
16)



3-(4-chlorophenyl)-4-[4-(methylsulfonyl)phenyl]-2(3H)-oxazolone,

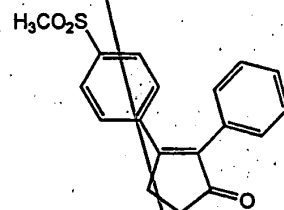
5

17)



4-[3-(4-fluorophenyl)-2,3-dihydro-2-oxo-4-oxazolyl]benzenesulfonamide,

18)



10

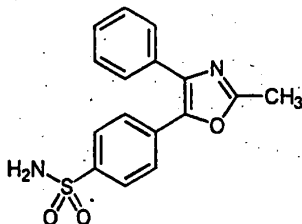
3-[4-(methylsulfonyl)phenyl]-2-phenyl-2-cyclopenten-1-one,

098600501

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-323-

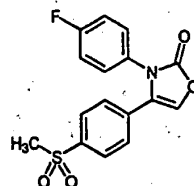
19)



4-(2-methyl-4-phenyl-5-oxazolyl)benzenesulfonamide,

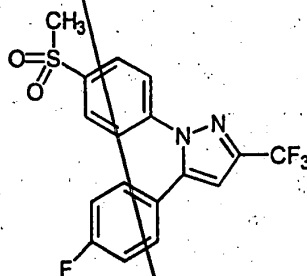
5

20)



3-(4-fluorophenyl)-4-[4-(methylsulfonyl)phenyl]-2(3H)-oxazolone,

21)



10

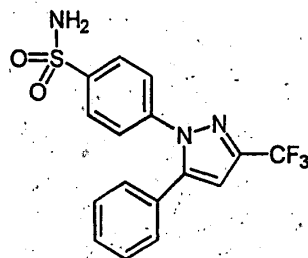
5-(4-fluorophenyl)-1-[4-(methylsulfonyl)phenyl]-3-(trifluoromethyl)-1H-pyrazole,

TO5001-20000000

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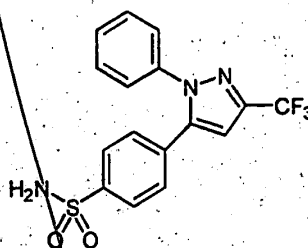
-324-

22)



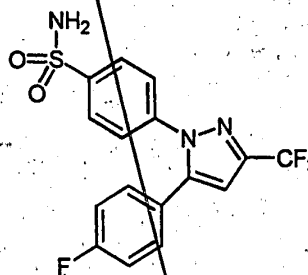
4-[5-phenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide,

5 23)



4-[1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]benzenesulfonamide,

24)

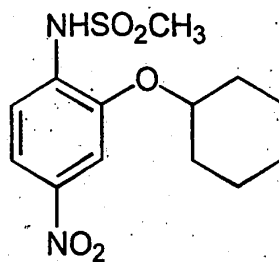


4-[5-(4-fluorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide,

10

-325-

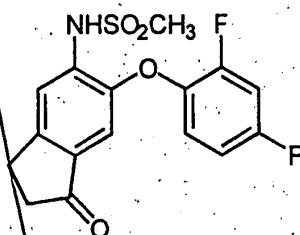
25)



N-[2-(cyclohexyloxy)-4-nitrophenyl]methanesulfonamide,

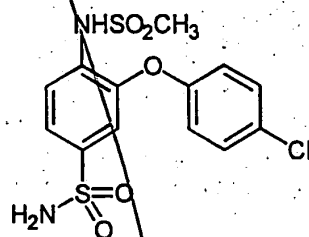
5

26)



N-[6-(2,4-difluorophenoxy)-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,

271



3-(4-chlorophenoxy)-4-
[(methylsulfonyl)amino]benzenesulfonamide,

10

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Cont

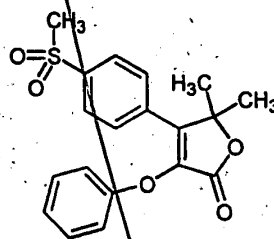
-326-

CC(=O)NSc1ccc(cc1)S(=O)(=O)N

5

CN(C)C1=CN=C(Sc2ccc(cc2)S(=O)(=O)N)C=C1

30)

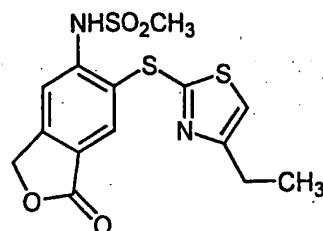


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-327-

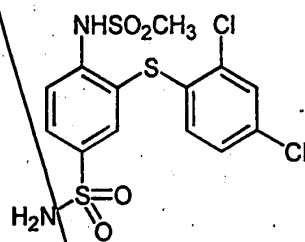
31)



N-[6-[(4-ethyl-2-thiazolyl)thio]-1,3-dihydro-1-oxo-5-isobenzofuranyl]methanesulfonamide,

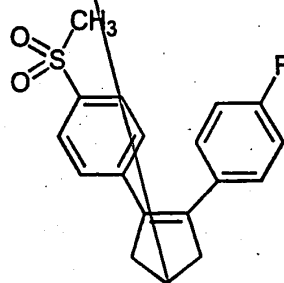
5

32)



3-[(2,4-dichlorophenyl)thio]-4-[(methanesulfonyl)amino]benzenesulfonamide,

33)



1-fluoro-4-[2-[4-(methanesulfonyl)phenyl]cyclopenten-1-yl]benzene,

10

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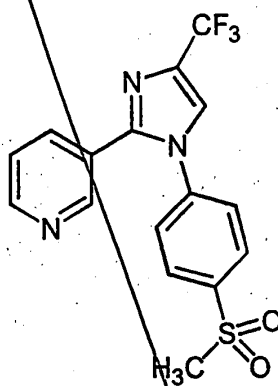
Sub 1 Cont

-328-

Clc1ccc(cc1)c2cc(C(F)F)nn2Nc3ccc(cc3)S(=O)(=O)N

5

35)

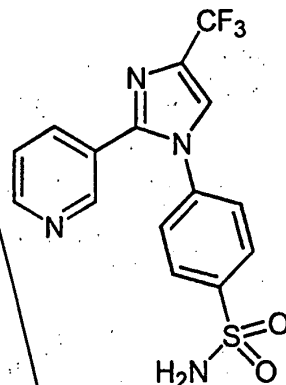


3-[1-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)-1H-imidazol-2-yl]pyridine,

105007-100504
0008063
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-329-

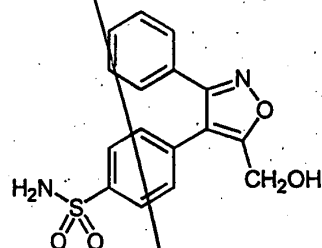
36)



4-[2-(3-pyridinyl)-4-(trifluoromethyl)-1H-imidazol-1-yl]benzenesulfonamide,

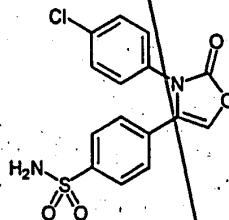
5

37)



4-[5-(hydroxymethyl)-3-phenylisoxazol-4-yl]benzenesulfonamide,

38)

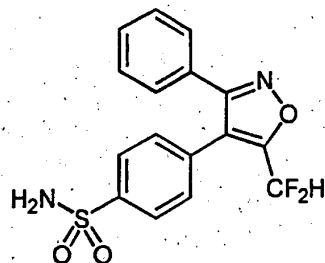


10

4-[3-(4-chlorophenyl)-2,3-dihydro-2-oxo-4-oxazolyl]benzenesulfonamide,

-330-

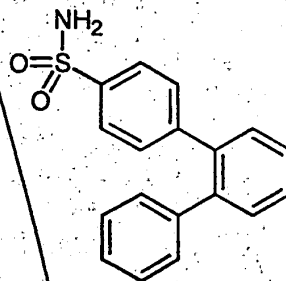
39)



4-[5-(difluoromethyl)-3-phenylisoxazol-4-yl]benzenesulfonamide,

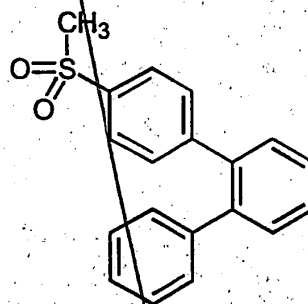
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40)



[1,1':2',1''-terphenyl]-4-sulfonamide,

41)

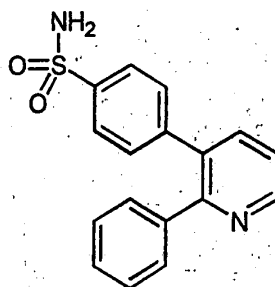


10

4-(methylsulfonyl)-1,1',2,1''-terphenyl,

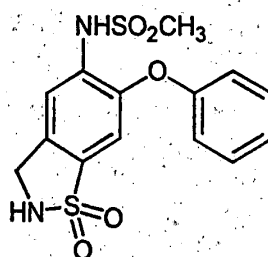
-331-

42)



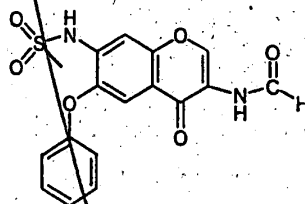
4-(2-phenyl-3-pyridinyl)benzenesulfonamide,

43)



N-(2,3-dihydro-1,1-dioxido-6-phenoxy-1,2-benzisothiazol-5-yl)methanesulfonamide, and

44)



N-[3-(formylamino)-4-oxo-6-phenoxy-4H-1-benzopyran-7-yl]methanesulfonamide,

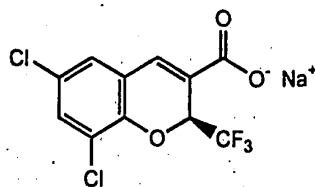
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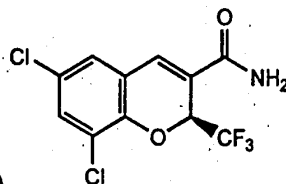
10

-332-

45)

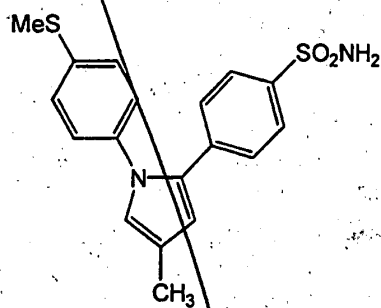


46)



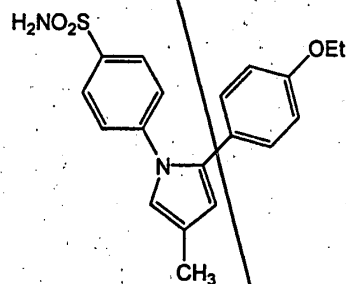
5

47)



, and

48)

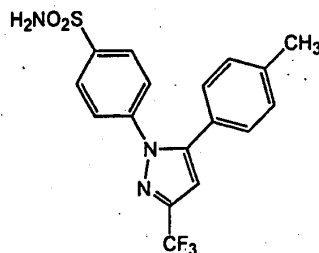


35. The method of Claim 1 wherein the
 10 cyclooxygenase-2 inhibitor is 5-chloro-3-(4-
 (methylsulfonyl)phenyl)-2-(methyl-5-pyridinyl)pyridine.

-333-

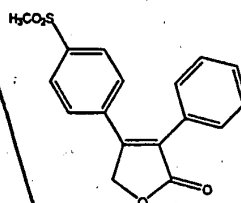
36. The method of Claim 1 wherein the cyclooxygenase-2 inhibitor is 2-(3,5-difluorophenyl)-3-(4-(methylsulfonyl)phenyl)-2-cyclopenten-1-one.

37. The method of Claim 1 wherein the
5 cyclooxygenase-2 inhibitor is



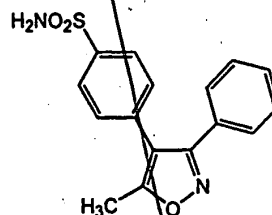
4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]-benzenesulfonamide.

38. The method of Claim 1 wherein the
10 cyclooxygenase-2 inhibitor is



rofecoxib, 4-(4-(methylsulfonyl)phenyl)-3-phenyl-2(5H)-furanone.

15 39. The method of Claim 1 wherein the
cyclooxygenase-2 inhibitor is



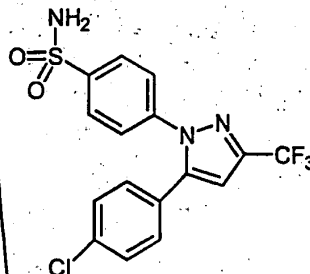
4-(5-methyl-3-phenylisoxazol-4-yl)benzenesulfonamide.

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40. The method of Claim 1 wherein the cyclooxygenase-2 inhibitor is N-[[4-(5-methyl-3-phenylisoxazol-4-yl)phenyl]sulfonyl]propanamide.

41. The method of Claim 1 wherein the
5 cyclooxygenase-2 inhibitor is



4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazole-1-yl]benzenesulfonamide.

42. The method of Claim 1 wherein the neoplasia is
10 selected from the group consisting of lung cancer,
breast cancer, gastrointestinal cancer, bladder cancer,
head and neck cancer and cervical cancer.

43. The method of Claim 1 wherein the neoplasia is selected from the group consisting of acral lentiginous melanoma, actinic keratoses, adenocarcinoma, adenoid cystic carcinoma, adenomas, adenosarcoma, adenosquamous carcinoma, astrocytic tumors, Bartholin's gland carcinoma, basal cell carcinoma, bronchial gland carcinomas, capillary, carcinoids, carcinoma, carcinosarcoma, cavernous, cholangiocarcinoma, chondrosarcoma, choroid plexus papilloma/carcinoma, clear cell carcinoma, cystadenoma, endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, ependymal, epithelioid, Ewing's sarcoma, fibrolamellar, focal nodular hyperplasia, gastrinoma, germ cell tumors, glioblastoma, glucagonoma,

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-335-

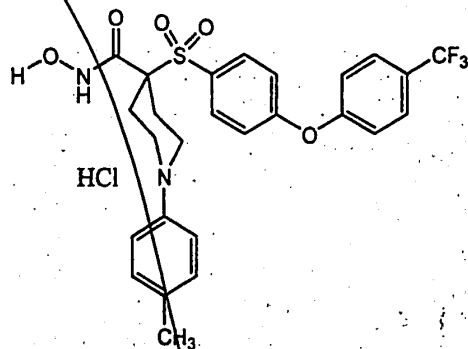
hemangiblastomas, hemangioendothelioma, hemangiomas,
hepatic adenoma, hepatic adenomatosis, hepatocellular
carcinoma, insulinoma, intraepithelial neoplasia,
interepithelial squamous cell neoplasia, invasive
5 squamous cell carcinoma, large cell carcinoma,
leiomyosarcoma, lentigo maligna melanomas, malignant
melanoma, malignant mesothelial tumors, medulloblastoma,
medulloepithelioma, melanoma, meningeal, mesothelial,
metastatic carcinoma, mucoepidermoid carcinoma,
10 neuroblastoma, neuroepithelial adenocarcinoma nodular
melanoma, oat cell carcinoma, oligodendroglial,
osteosarcoma, pancreatic polypeptide, papillary serous
adenocarcinoma, pineal cell, pituitary tumors,
plasmacytoma, pseudosarcoma, pulmonary blastoma, renal
15 cell carcinoma, retinoblastoma, rhabdomyosarcoma,
sarcoma, serous carcinoma, small cell carcinoma, soft
tissue carcinomas, somatostatin-secreting tumor,
squamous carcinoma, squamous cell carcinoma,
submesothelial, superficial spreading melanoma,
20 undifferentiated carcinoma, uveal melanoma, verrucous
carcinoma, vipoma, well differentiated carcinoma, and
Wilm's tumor.

44. The method of Claim 1 wherein the matrix
25 metalloproteinase inhibitor is selected from compounds,
and their pharmaceutically acceptable salts thereof, of
the group consisting of:

FOUO-10501

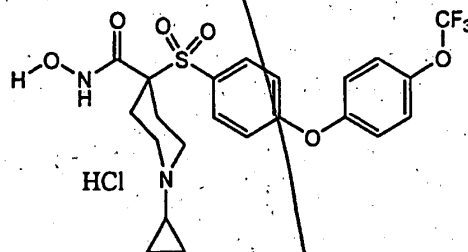
-336-

1)



N-hydroxy-1-(4-methylphenyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

2)

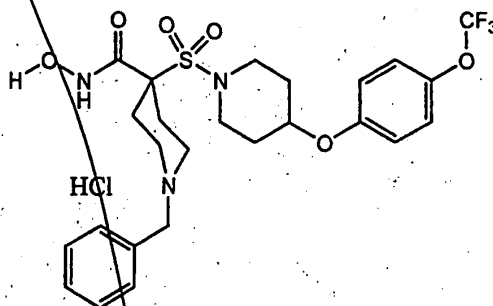


1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

Sub 1
cont
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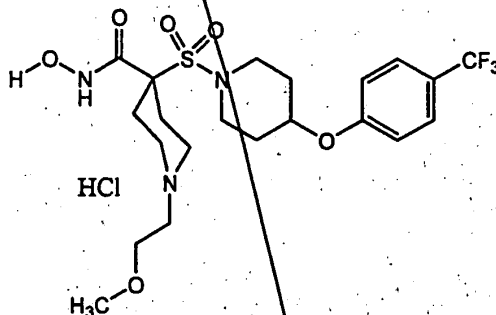
-337-

3)



N-hydroxy-1-(phenylmethyl)-4-[[4-[4-(trifluoromethoxy)phenoxy]-1-piperidinyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

4)

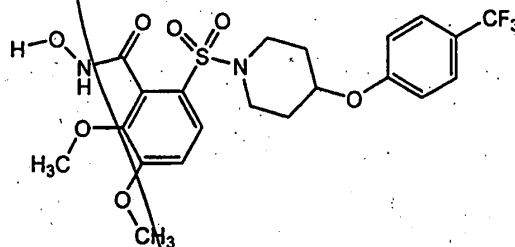


N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

Suba Cont

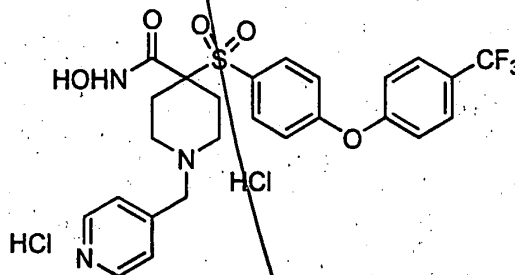
-338-

5)



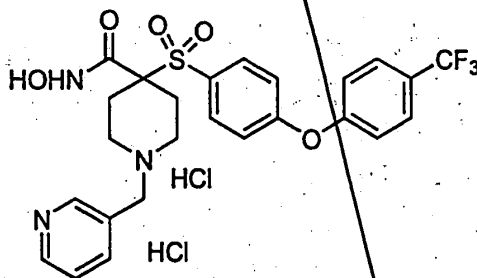
N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide;

6)



N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

7)



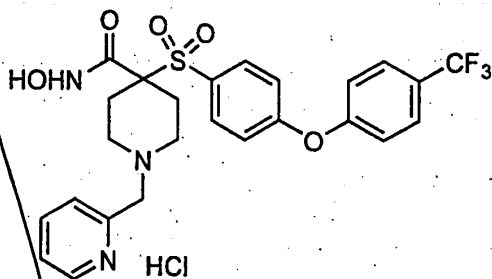
N-hydroxy-1-(3-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

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See a Cont

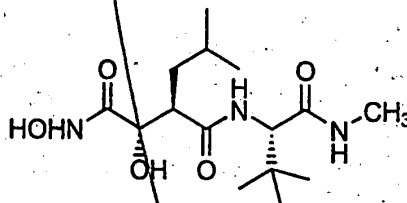
-339-

8)



N-hydroxy-1-(2-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

9)



British Biotech BB-2516 (Marimastat), N4-[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1,2-dihydroxy-3 (2-methylpropyl)-, [2S-[N4(R*),2R*,3S*]]-),

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-340-

O=C(O)C(CS1=CC=CC=C1)CC(=O)C2=CC=C(C=C2)-C3=CC=C(C=C3)C

5

CC1(C)CCN(C1)C(=O)O.N#Cc1ccc(Oc2ccc(S(=O)(=O)c3ccc(N4CCSC4(C)C)cc3)cc2)cc1

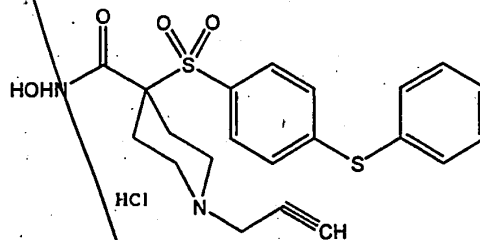
10

15

13) Chiroscience D-2163, 2- [1S- ([(2R,S)-
acetylmercapto- 5- phthalimido]pentanoyl- L-
leucyl)amino- 3- methylbutyl]imidazole,

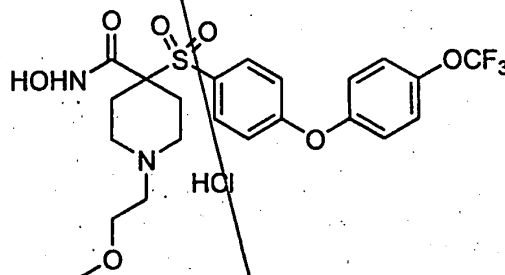
-341-

14)



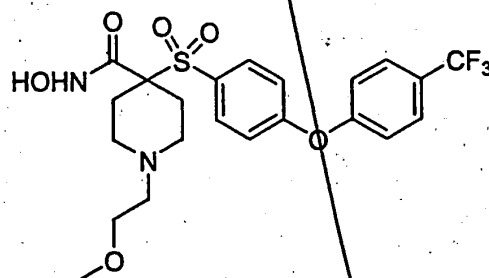
N-hydroxy-4-[[4-(phenylthio)phenyl]sulfonyl]-
1-(2-propynyl)-4-piperidinecarboxamide
monohydrochloride,

15)



N-hydroxy-1-(2-methoxyethyl)-4-[[4-[4-
(trifluoromethoxy) phenoxy]phenyl]sulfonyl]-4-
piperidinecarboxamide monohydrochloride,

16)

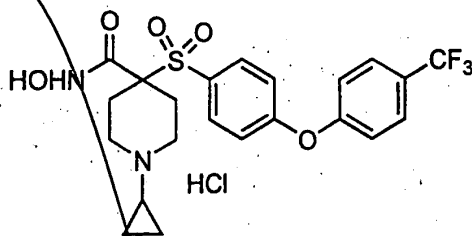


N-hydroxy-1-(2-methoxyethyl)-4-[[4-[4-
(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-
piperidinecarboxamide,

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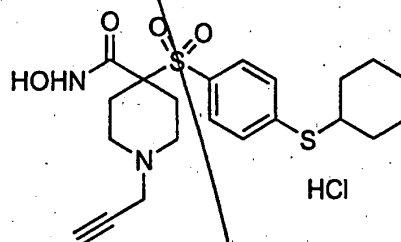
-342-

17)



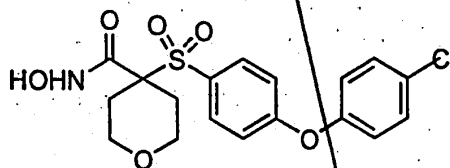
1-cyclopropyl-N-hydroxy-4-[[4-[(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

18)



4-[[4-(cyclohexylthio)phenyl]sulfonyl]-N-hydroxy-1-(2-propynyl)-4-piperidinecarboxamide monohydrochloride,

19)

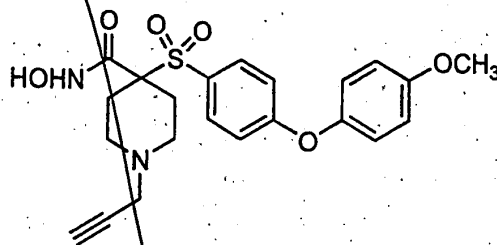


4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-N-hydroxy-2H-pyran-4-carboxamide,

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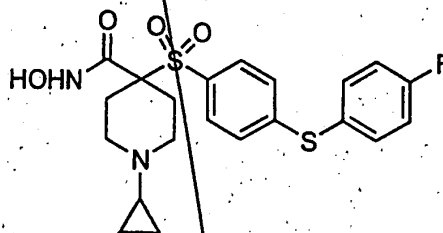
-343-

20)



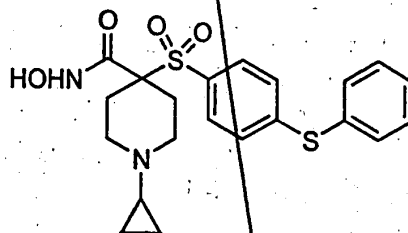
N-hydroxy-4-([4-(4-methoxyphenoxy)phenyl]sulfonyl)-1-(2-propynyl)-4-piperidinecarboxamide,

21)



1-cyclopropyl-4-([4-([4-(4-fluorophenyl)thio]phenyl)sulfonyl]-N-hydroxy-4-piperidinecarboxamide,

22)

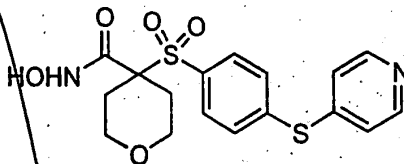


1-cyclopropyl-N-hydroxy-4-([4-(phenylthio)phenyl]sulfonyl)-4-piperidinecarboxamide,

TO5001-10089860
Sub a cont

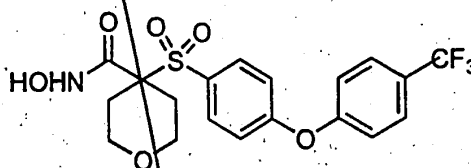
-344-

23)



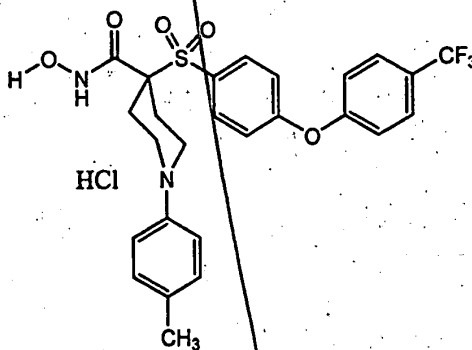
tetrahydro-N-hydroxy-4-[[4-(4-pyridinylthio)phenyl]sulfonyl]-2H-pyran-4-carboxamide and

24)



tetrahydro-N-hydroxy-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-2H-pyran-4-carboxamide.

45. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is



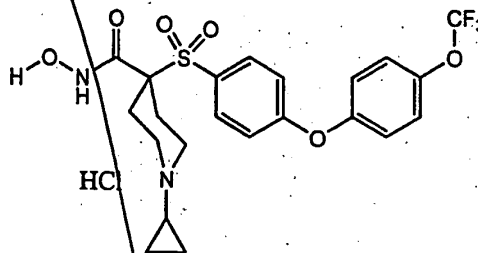
N-hydroxy-1-(4-methylphenyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

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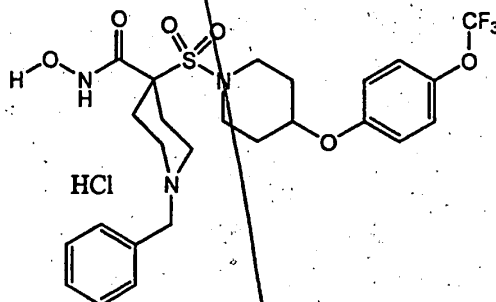
-345-

46. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is



1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

47. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is

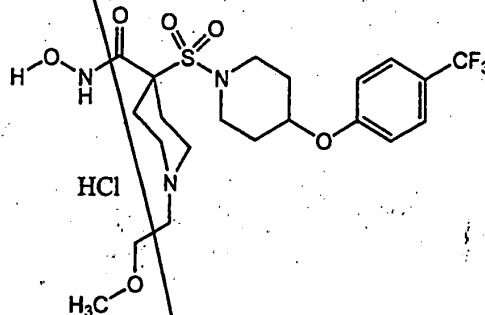


N-hydroxy-1-(phenylmethyl)-4-[[4-[4-(trifluoromethoxy)phenoxy]-1-piperidinyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

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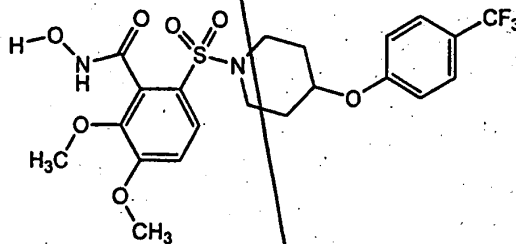
Sub a cont

48. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is



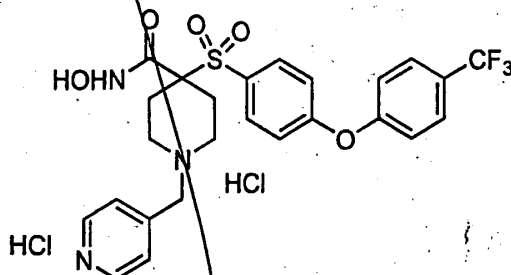
N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

49. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is



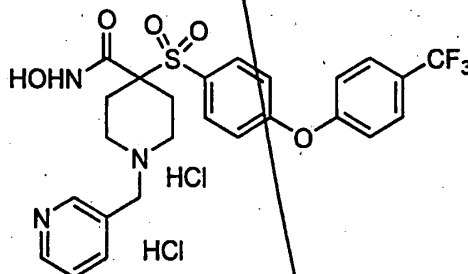
N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide.

50. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is



5 N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

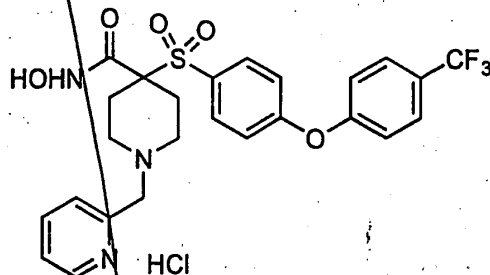
51. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is



15 N-hydroxy-1-(3-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

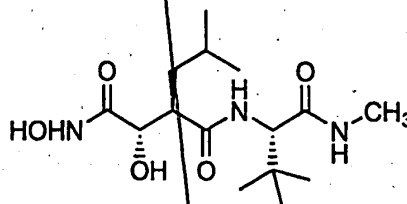
-348-

52. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is



N-hydroxy-1-(2-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

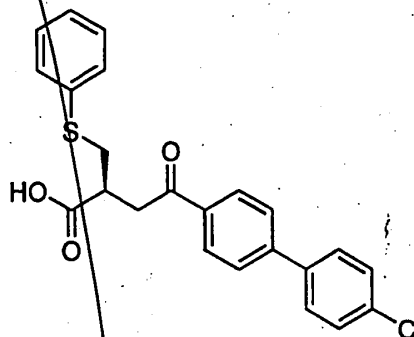
53. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is



British Biotech BB-2516 (Marimastat), N4-[2,2-dimethyl- 1-[(methylamino)carbonyl]propyl]-N1,2 -dihydroxy-3 (2- methylpropyl)-, [2S-[N4(R*),2R*,3S*]]-).

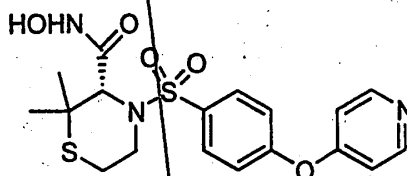
-349-

54. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is



5 Bayer Ag Bay-12-9566, 4-[(4'-chloro[1,1'-
iphenyl]-4-yl)oxy]-2-
[(phenylthio)methyl]butanoic acid.

55. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is



15 Agouron Pharmaceuticals AG-3340, N-hydroxy-
2,2-dimethyl-4-[[4-(4-
pyridinyloxy)phenyl]sulfonyl]-3-
thiomorpholinecarboxamide.

56. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is CollaGenex
Pharmaceuticals CMT-3 (Metastat), 6-demethyl-6-deoxy-4-
20 dedimethylaminotetracycline.

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-350-

57. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is Chiroscience D-2163, 2-[1S- ((2R,S)- acetylmercapto- 5- phthalimido]pentanoyl-L-leucyl)amino- 3- methylbutyl]imidazole.

5

58. A method for treating or preventing a neoplasia disorder in a mammal in need of such treatment or prevention, which method comprises administering to said mammal a therapeutically-effective amount of a combination of radiation, a cyclooxygenase-2 inhibitor, a matrix metalloproteinase inhibitor, and an antineoplastic agent, wherein said antineoplastic agent is selected from the group consisting of anastrozole, calcium carbonate, capecitabine, carboplatin, cisplatin, Cell Pathways CP-461, docetaxel, doxorubicin, etoposide, fluorouracil (5-FU), fluoxymestrine, gemcitabine, goserelin, irinotecan, ketoconazole, letrozol, leucovorin, levamisole, megestrol, mitoxantrone, paclitaxel, raloxifene, retinoic acid, tamoxifen, thiotepa, topotecan, toremifene, vinorelbine, vinblastine, vincristine, selenium (selenomethionine), ursodeoxycholic acid, sulindac sulfone, exemestane and eflornithine (DFMO).

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59. The method of Claim 58 wherein the combination is administered in a sequential manner.

60. The method of Claim 58 wherein the combination is administered in a substantially simultaneous manner.

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-351-

61. The method of Claim 58 wherein the antineoplastic agent is capecitabine.

62. The method of Claim 58 wherein the
5 antineoplastic agent is carboplatin.

63. The method of Claim 58 wherein the antineoplastic agent is cisplatin.

10 64. The method of Claim 58 wherein the
antineoplastic agent is Cell Pathways CP-461.

65. The method of Claim 58 wherein the antineoplastic agent is docetaxel.

66. The method of Claim 58 wherein the antineoplastic agent is doxorubicin.

67. The method of Claim 58 wherein the
20 antineoplastic agent is etoposide.

68. The method of Claim 58 wherein the antineoplastic agent is fluoxymestrine.

25 69. The method of Claim 58 wherein the
antineoplastic agent is gemcitabine.

70. The method of Claim 58 wherein the antineoplastic agent is goserelin.

71. The method of Claim 58 wherein the antineoplastic agent is irinotecan.

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cont

-352-

72. The method of Claim 58 wherein the antineoplastic agent is ketoconazole.

5 73. The method of Claim 58 wherein the
antineoplastic agent is letrozol.

74. The method of Claim 58 wherein the antineoplastic agent is leucovorin.

10

75. The method of Claim 58 wherein the antineoplastic agent is levamisole.

76. The method of Claim 58 wherein the
15 antineoplastic agent is megestrol.

77. The method of Claim 58 wherein the antineoplastic agent is mitoxantrone.

20 78. The method of Claim 58 wherein the
 antineoplastic agent is paclitaxel.

79. The method of Claim 58 wherein the antineoplastic agent is raloxifene.

25

80. The method of Claim 58 wherein the antineoplastic agent is retinoid acid.

81. The method of Claim 58 wherein the
30 antineoplastic agent is tamoxifen

-353-

82. The method of Claim 58 wherein the antineoplastic agent is thiotepa.

83. The method of Claim 58 wherein the antineoplastic agent is topotecan.

84. The method of Claim 58 wherein the antineoplastic agent is toremifene.

85. The method of Claim 58 wherein the antineoplastic agent is vinorelbine.

86. The method of Claim 58 wherein the antineoplastic agent is vinblastine.

87. The method of Claim 58 wherein the antineoplastic agent is vincristine.

88. The method of Claim 58 wherein the antineoplastic agent is selenium (selenomethionine).

89. The method of Claim 58 wherein the antineoplastic agent is sulindac sulfone.

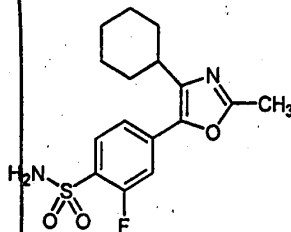
90. The method of Claim 58 wherein the antineoplastic agent is eflornithine (DFMO).

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-354-

91. The method of Claim 58 wherein the cyclooxygenase-2 inhibitor is selected from compounds, and their pharmaceutically acceptable salts thereof, of the group consisting of:

5 1)



JTE-522, 4-(4-cyclohexyl-2-methyloxazol-5-yl)-2-fluorobenzenesulfonamide,

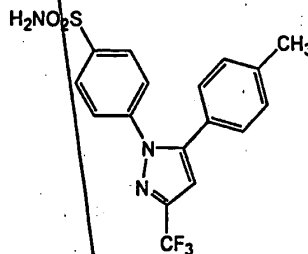
10 2)

5-chloro-3-(4-(methylsulfonyl)phenyl)-2-(methyl-5-pyridinyl)pyridine,

3)

2-(3,5-difluorophenyl)-3-(4-(methylsulfonyl)phenyl)-2-cyclopenten-1-one,

15 4)

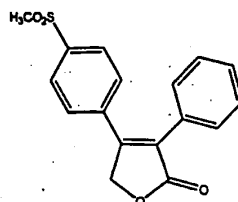


4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]-benzenesulfonamide,

Supp. Cont.
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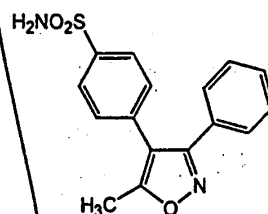
5)



rofecoxib, 4-(4-(methylsulfonyl)phenyl)-3-phenyl-2(5H)-furanone,

5

6)



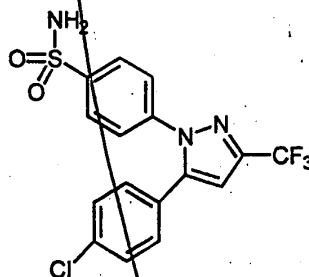
4-(5-methyl-3-phenylisoxazol-4-yl)benzenesulfonamide,

7)

N-[[4-(5-methyl-3-phenylisoxazol-4yl)phenyl]sulfonyl]propanamide,

10

8)

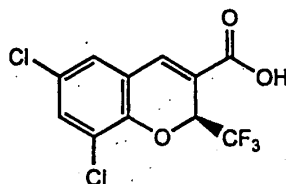


4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazole-1-yl]benzenesulfonamide,

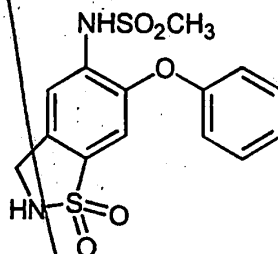
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-356-

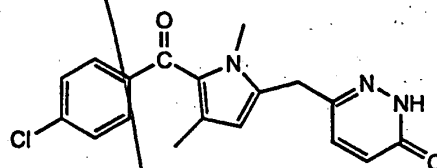
9)



10)

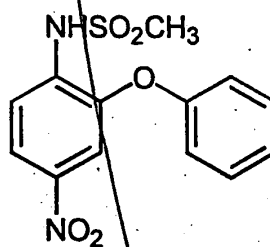


11)



6-[[5-(4-chlorobenzoyl)-1,4-dimethyl-1H-pyrrol-2-yl]methyl]-3(2H)-pyridazinone,

12)



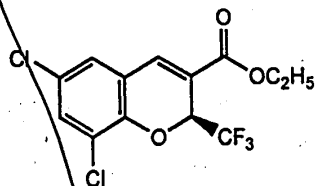
N-(4-nitro-2-phenoxyphenyl)methanesulfonamide,

Supp. Cont
T0500T-9900050

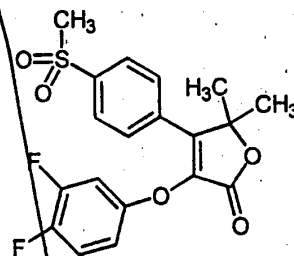
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-357-

13)

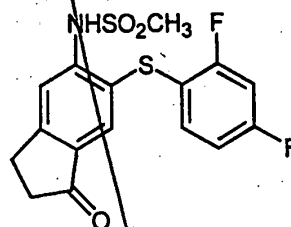


14)



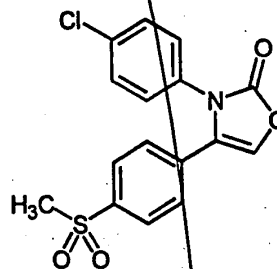
3-(3,4-difluorophenoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-2(5H)-furanone,

15)



N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,

16)

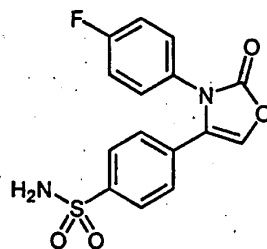


3-(4-chlorophenyl)-4-[4-(methylsulfonyl)phenyl]-2(3H)-oxazolone,

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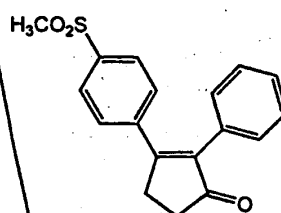
-358-

17)



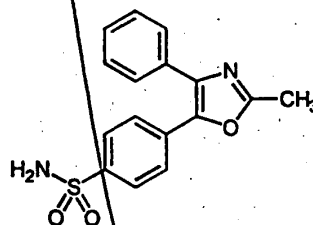
4-[3-(4-fluorophenyl)-2,3-dihydro-2-oxo-4-oxazolyl]benzenesulfonamide,

18)



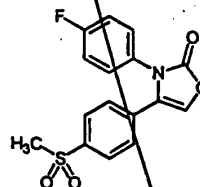
3-[4-(methanesulfonyl)phenyl]-2-phenyl-2-cyclopenten-1-one,

19)



4-(2-methyl-4-phenyl-5-oxazolyl)benzenesulfonamide,

20)

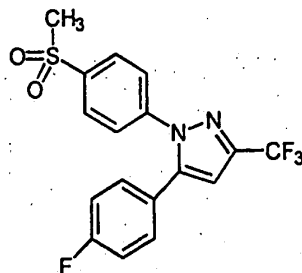


3-(4-fluorophenyl)-4-[4-(methanesulfonyl)phenyl]-2(3H)-oxazolone,

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Cont

-359-

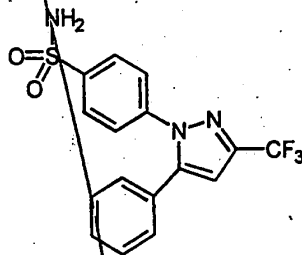
21)



5-(4-fluorophenyl)-1-[4-(methylsulfonyl)phenyl]-3-(trifluoromethyl)-1H-pyrazole,

5

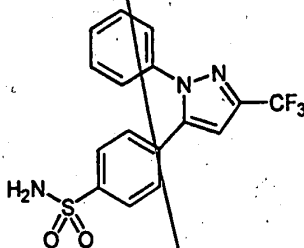
22)



4-[5-phenyl]-3-(trifluoromethyl)-1H-pyrazol-1-yl benzenesulfonamide,

10

23)



4-[1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl] benzenesulfonamide,

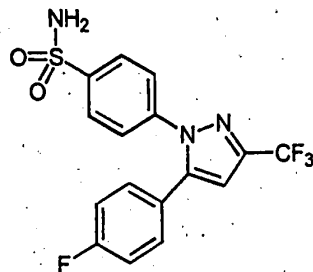
15

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Sub 1
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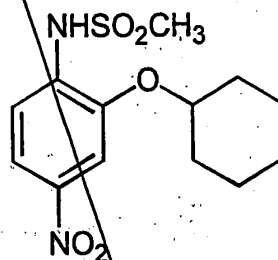
-360-

24)



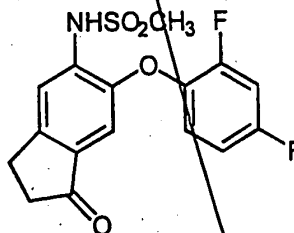
4-[5-(4-fluorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide,

25)



N-[2-(cyclohexyloxy)-4-nitrophenyl]methanesulfonamide,

26)

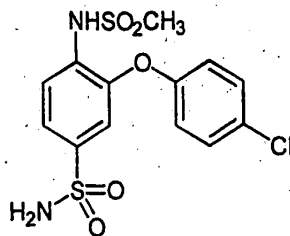


N-[6-(2,4-difluorophenoxy)-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,

Supp
a
cont

-361-

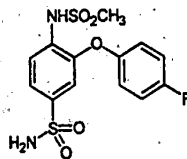
27)



3-(4-chlorophenoxy)-4-
[(methylsulfonyl)amino]benzenesulfonamide,

5

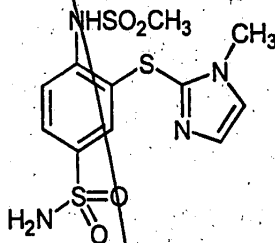
28)



3-(4-fluorophenoxy)-4-
[(methylsulfonyl)amino]benzenesulfonamide,

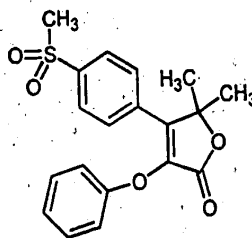
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29)



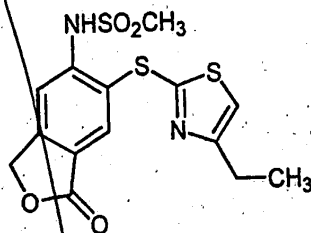
3-[(1-methyl-1H-imidazol-2-yl)thio]-4-
[(methylsulfonyl) amino]benzenesulfonamide,

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cont



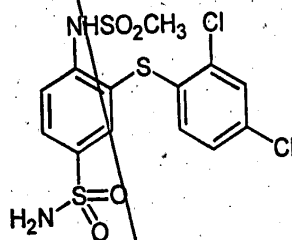
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31)



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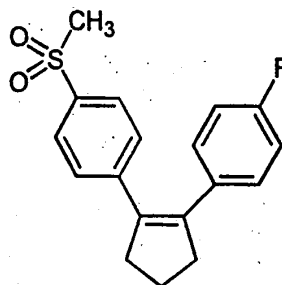
32)



3-[(2,4-dichlorophenyl)thio]-4-
[(methylsulfonyl)amino]benzenesulfonamide,

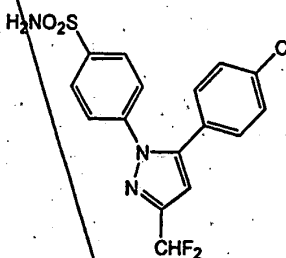
-363-

33)



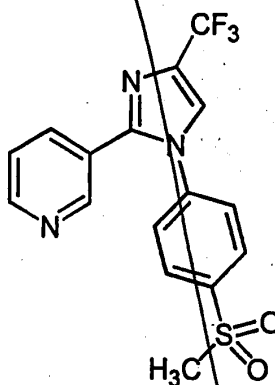
1-fluoro-4-[2-[4-(methylsulfonyl)phenyl]cyclopenten-1-yl]benzene,

34)



4-[5-(4-chlorophenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide,

35)



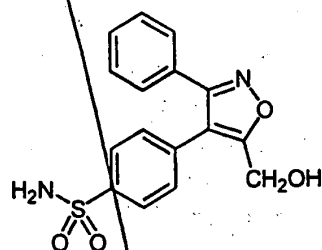
3-[1-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)-1H-imidazol-2-yl]pyridine,

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0466063:100501

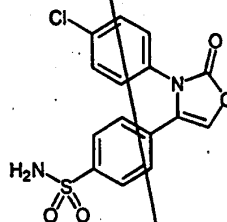
-364-

Nc1ccc(cc1n1cc(C2=CC=CC=C2)c3cc(C(F)(F)F)cn31)c4cccnc4

37)



38)



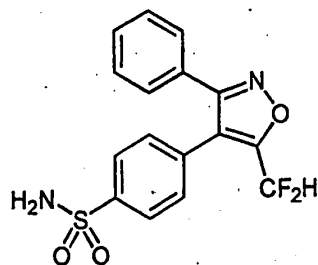
4-[3-(4-chlorophenyl)-2,3-dihydro-2-oxo-4-oxazolyl]benzenesulfonamide,

10

~~0066813-00501~~

-365-

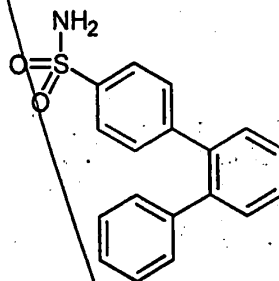
39)



4-[5-(difluoromethyl)-3-phenylisoxazol-4-yl]benzenesulfonamide,

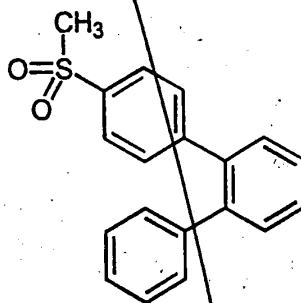
5

40)



[1,1':2',1''-terphenyl]-4-sulfonamide,

41)



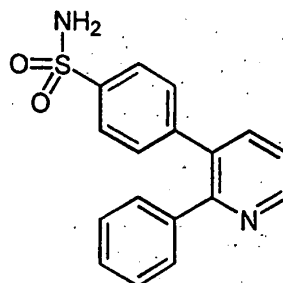
4-(methylsulfonyl)-1,1',2',1''-terphenyl,

10

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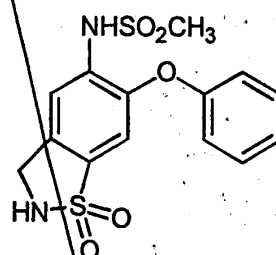
-366-

42)



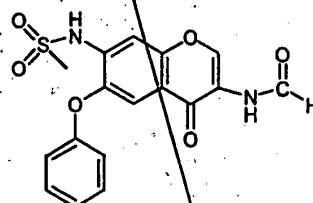
4-(2-phenyl-3-pyridinyl)benzenesulfonamide,

43)



N-(2,3-dihydro-1,1-dioxido-6-phenoxy-1,2-benzisothiazol-5-yl)methanesulfonamide, and

44)

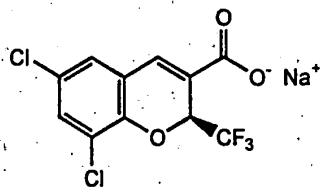


N-[3-(formylamino)-4-oxo-6-phenoxy-4H-1-benzopyran-7-yl]methanesulfonamide,

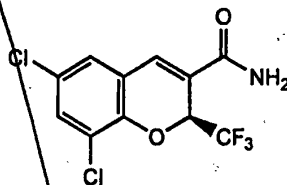
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-367-

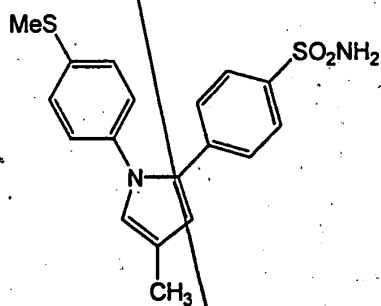
45)



46)

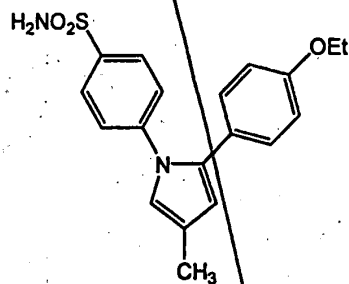


47)



and

48)

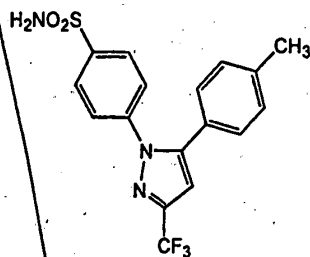


92. The method of Claim 58 wherein the
10 cyclooxygenase-2 inhibitor is 5-chloro-3-(4-
(methylsulfonyl)phenyl)-2-(methyl-5-pyridinyl)pyridine.

-368-

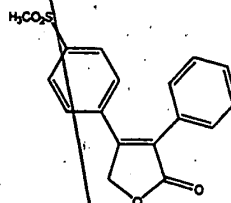
93. The method of Claim 58 wherein the cyclooxygenase-2 inhibitor is 2-(3,5-difluorophenyl)-3-4-(methylsulfonyl)phenyl)-2-cyclopenten-1-one.

94. The method of Claim 58 wherein the cyclooxygenase-2 inhibitor is



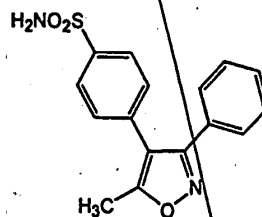
4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]-benzenesulfonamide.

95. The method of Claim 58 wherein the cyclooxygenase-2 inhibitor is



rofecoxib, 4-(4-(methylsulfonyl)phenyl)-3-phenyl-2(5H)-furanone.

96. The method of Claim 58 wherein the cyclooxygenase-2 inhibitor is



4-(5-methyl-3-phenylisoxazol-4-yl)benzenesulfonamide.

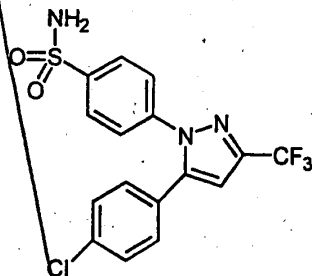
T05001-20084860

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97. The method of Claim 58 wherein the cyclooxygenase-2 inhibitor is N-[[4-(5-methyl-3-phenylisoxazol-4-yl)phenyl]sulfonyl]propanamide.

98. The method of Claim 58 wherein the cyclooxygenase-2 inhibitor is



4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazole-1-yl]benzenesulfonamide.

99. The method of Claim 58 wherein the neoplasia is selected from the group consisting of lung cancer, breast cancer, gastrointestinal cancer, bladder cancer, head and neck cancer and cervical cancer.

100. The method of Claim 58 wherein the neoplasia is selected from the group consisting of acral lentiginous melanoma, actinic keratoses, adenocarcinoma, adenoid cystic carcinoma, adenomas, adenocarcinoma, adenosquamous carcinoma, astrocytic tumors, Bartholin gland carcinoma, basal cell carcinoma, bronchial gland carcinomas, capillary, carcinoids, carcinoma, carcinosarcoma, cavernous, cholangiocarcinoma, chondrosarcoma, choroid plexus papilloma/carcinoma, clear cell carcinoma, cystadenoma, endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, ependymal, epitheloid, Ewing's sarcoma, fibrolamellar, focal nodular hyperplasia, gastrinoma, germ cell tumors, glioblastoma,

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-370-

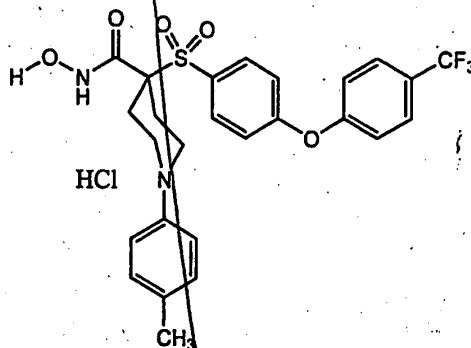
- glucagonoma, hemangiblastomas, hemangioendothelioma,
hemangiomas, hepatic adenoma, hepatic adenomatosis,
hepatocellular carcinoma, insulinoma, intraepithelial
neoplasia, interepithelial squamous cell neoplasia,
5 invasive squamous cell carcinoma, large cell carcinoma,
leiomyosarcoma, lentigo maligna melanomas, malignant
melanoma, malignant mesothelial tumors, medulloblastoma,
medulloepithelioma, melanoma, meningeal, mesothelial,
metastatic carcinoma, mucoepidermoid carcinoma,
10 neuroblastoma, neuroepithelial adenocarcinoma nodular
melanoma, oat cell carcinoma, oligodendroglial,
osteosarcoma, pancreatic polypeptide, papillary serous
adenocarcinoma, pineal cell, pituitary tumors,
plasmacytoma, pseudosarcoma, pulmonary blastoma, renal
15 cell carcinoma, retinoblastoma, rhabdomyosarcoma,
sarcoma, serous carcinoma, small cell carcinoma, soft
tissue carcinomas, somatostatin-secreting tumor,
squamous carcinoma, squamous cell carcinoma,
submesothelial, superficial spreading melanoma,
20 undifferentiated carcinoma, uveal melanoma, verrucous
carcinoma, vipoma, well differentiated carcinoma, and
Wilm's tumor.

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-371-

101. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is selected from compounds, and their pharmaceutically acceptable salts thereof, of the group consisting of:

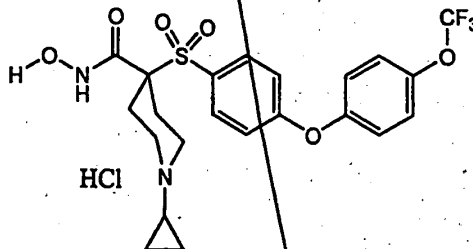
5 1)



N-hydroxy-1-(4-methylphenyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

10

2)



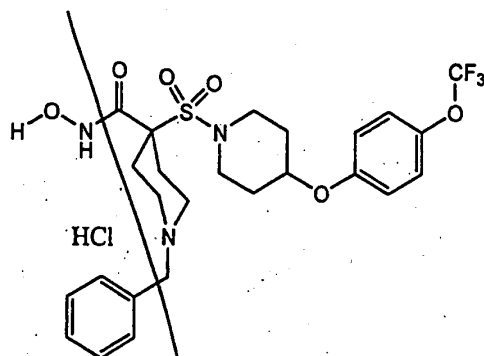
1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

15

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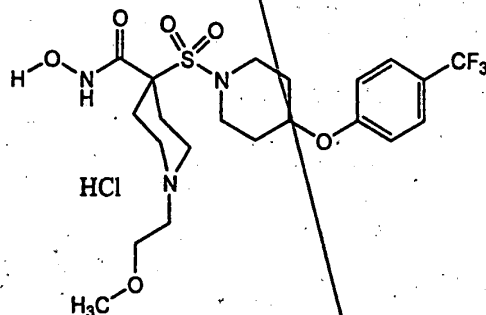
-372-

3)



N-hydroxy-1-(phenylmethyl)-4-[[4-[4-(trifluoromethoxy)phenoxy]-1-piperidinyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

4)

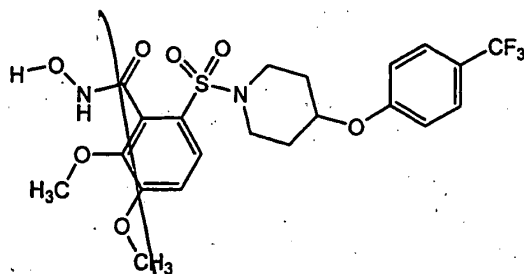


N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

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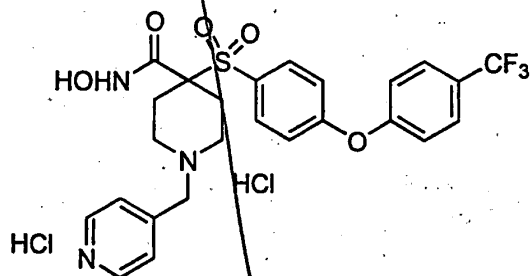
-373-

5)



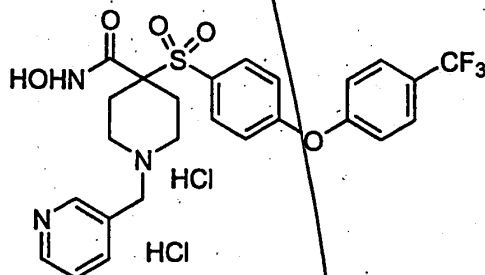
N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide,

6)



N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

7)



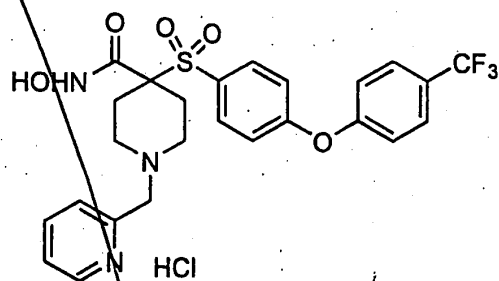
N-hydroxy-1-(3-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

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-374-

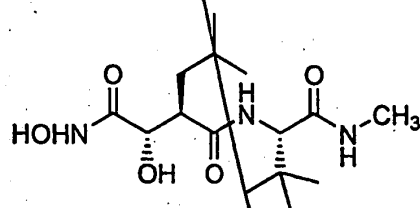
8)



5

N-hydroxy-1-(2-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

9)



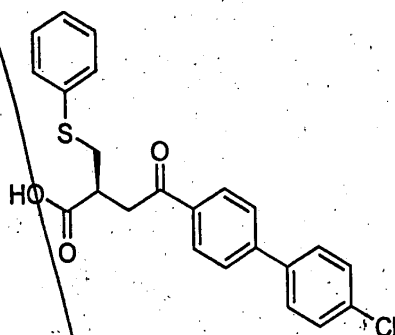
10

British Biotech BB-2516 (Marimastat), N4-[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1,2-dihydroxy-3-(2-methylpropyl)-, [2S-[N4(R*),2R*,3S*]]-),

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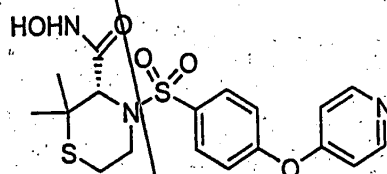
-375-

10)



Bayer Ag Bay-12-9566, 4-[(4'-chloro[1,1'-
 biphenyl]-4-yl)oxy]-2-
 [(phenylthio)methyl]butanoic acid,

11)



Agouron Pharmaceuticals AG-3340, N-hydroxy-2,2-
 dimethyl-4-[[4-(4-
 pyridinyloxy)phenyl]sulfonyl] 3-
 thiomorpholinecarboxamide,

12) CollaGenex Pharmaceuticals CMT-3 (Metastat),
 6-demethyl-6-deoxy-4-
 dedimethylaminotetracycline,

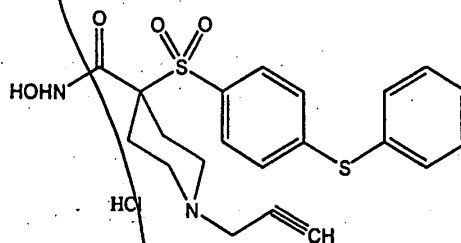
13) Chiroscience D-2163, 2- [1S- ((2R,S)-
 acetylmercapto- 5- phthalimido]pentanoyl- L-
 leucyl)amino- 3- methylbutyl]imidazole,

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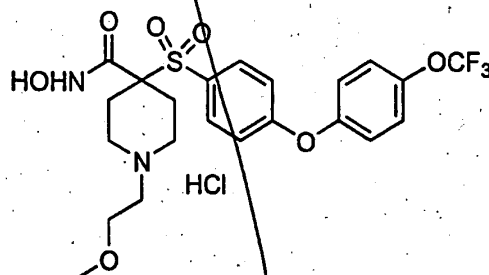
-376-

14)



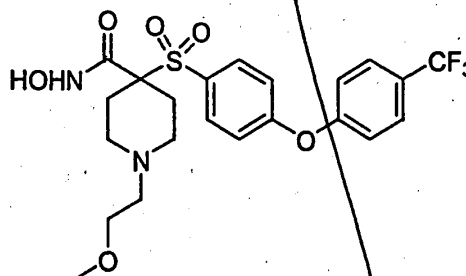
N-hydroxy-4-[[4-(phenylthio)phenyl]sulfonyl]-
1-(2-propynyl)-4-piperidinecarboxamide
monohydrochloride,

15)



N-hydroxy-1-(2-methoxyethyl)-4-[[4-[4-
(trifluoromethoxy) phenoxy]phenyl]sulfonyl]-4-
piperidinecarboxamide monohydrochloride,

16)

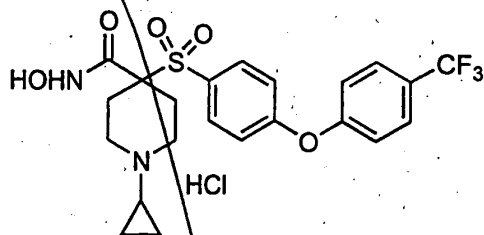


N-hydroxy-1-(2-methoxyethyl)-4-[[4-[4-
(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-
piperidinecarboxamide,

105001-29089860
See a Cont

-377-

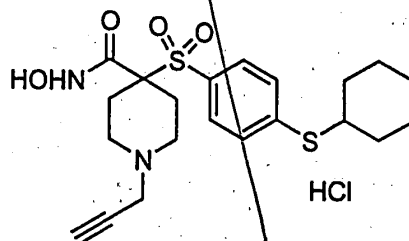
17)



1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

5

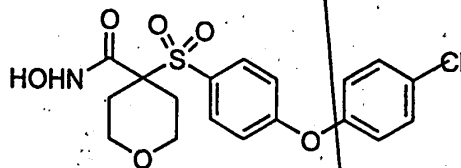
18)



4-[[4-(cyclohexylthio)phenyl]sulfonyl]-N-hydroxy-1-(2-propynyl)-4-piperidinecarboxamide monohydrochloride,

10

19)



4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-N-hydroxy-2H-pyran-4-carboxamide,

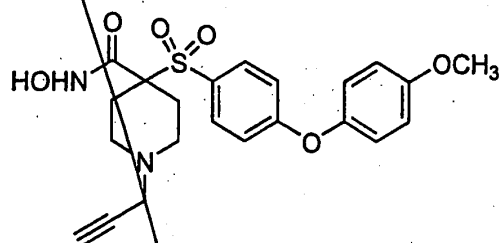
15

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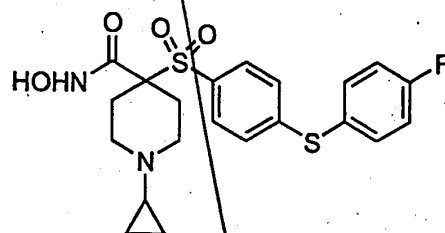
-378-

20)



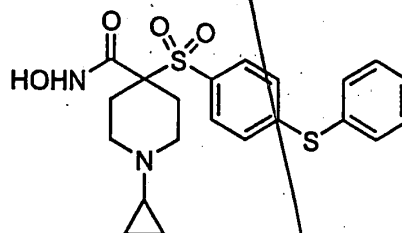
N-hydroxy-4-[[4-(4-methoxyphenoxy)phenyl]sulfonyl]-1-(2-propynyl)-4-piperidinecarboxamide,

21)



1-cyclopropyl-4-[[4-(4-fluorophenylthio)phenyl]sulfonyl]-N-hydroxy-4-piperidinecarboxamide,

22)

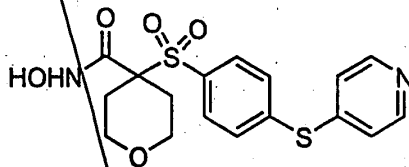


1-cyclopropyl-N-hydroxy-4-[[4-(phenylthio)phenyl]sulfonyl]-4-piperidinecarboxamide,

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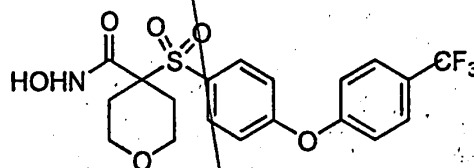
-379-

23)



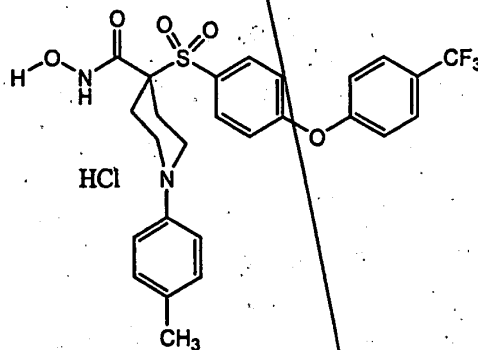
tetrahydro-N-hydroxy-4-[[4-(4-pyridinylthio)phenyl]sulfonyl]-2H-pyran-4-carboxamide, and

24)



tetrahydro-N-hydroxy-4-[[4-(4-(trifluoromethyl)phenoxy)phenyl]sulfonyl]-2H-pyran-4-carboxamide.

102. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is

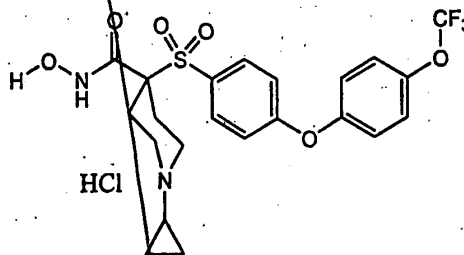


N-hydroxy-1-(4-methylphenyl)-4-[[4-(4-(trifluoromethyl)phenoxy)phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

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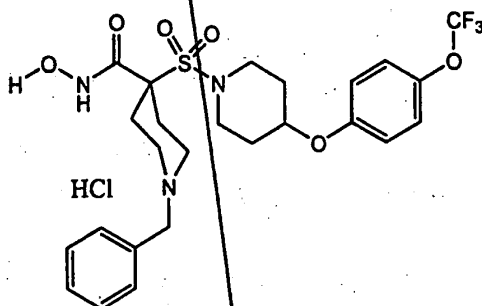
-380-

103. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is



1-cyclopropyl-N-hydroxy-4-[[4-[(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

104. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is



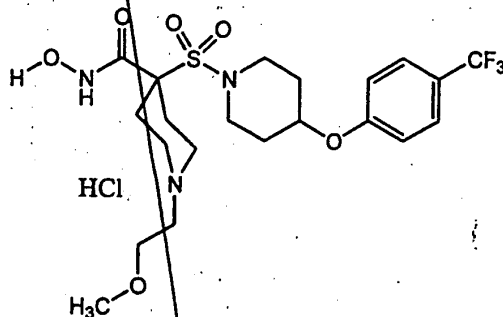
N-hydroxy-1-(phenylmethyl)-4-[[4-[(trifluoromethoxy)phenoxy]-1-piperidinyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

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See Cont

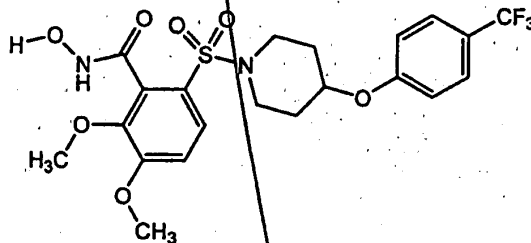
-381-

105. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is



N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

106. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is

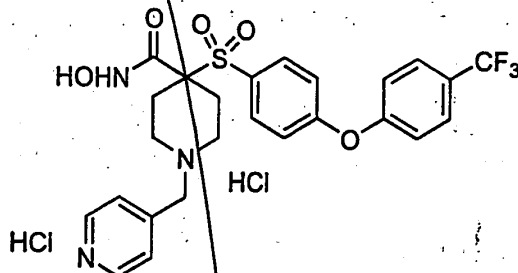


N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide.

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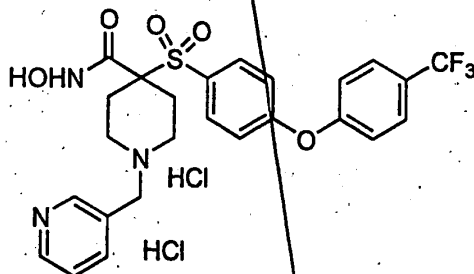
-382-

107. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is



5 N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

108. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is

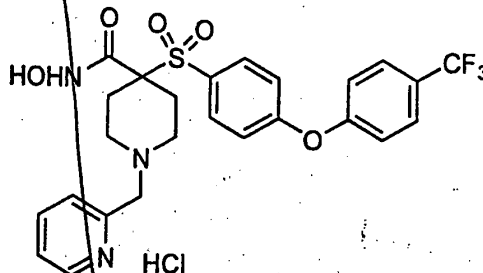


15 N-hydroxy-1-(3-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

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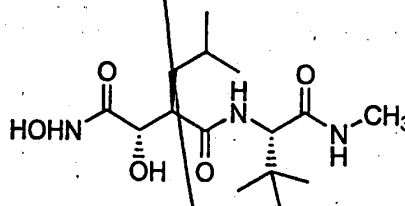
-383-

109. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is



N-hydroxy-1-(2-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

110. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is



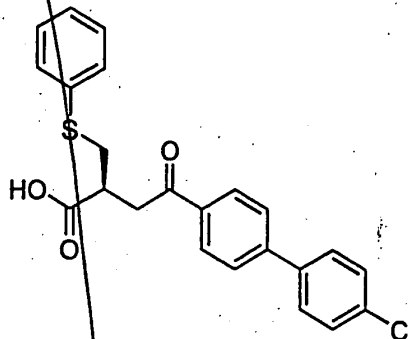
British Biotech BB-2516 (Marimastat), N4-[2,2-dimethyl- 1-[(methylamino)carbonyl]propyl]-N1,2 -dihydroxy-3 (2- methylpropyl)-, [2S-[N4(R*), 2R*, 3S*]]-).

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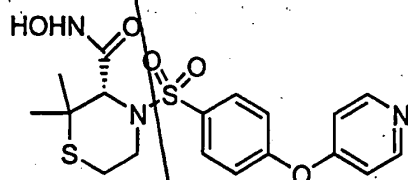
-384-

111. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is



5 Bayer Ag Bay-12-9566, 4-[(4'-chloro[1,1'-
iphenyl]-4-yl)oxy]-2-
[(phenylthio)methyl]butanoic acid.

112. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is



10 Agouron Pharmaceuticals AG-3340, N-hydroxy-
2,2-dimethyl-4-[[4-(4-
15 pyridinyloxy)phenyl]sulfonyl]-3-
thiomorpholinecarboxamide.

113. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is CollaGenex
Pharmaceuticals CMT-3 (Metastat), 6-demethyl-6-deoxy-4-
20 dedimethylaminotetracycline.

114. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is Chiroscience D-2163, 2-

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Cont

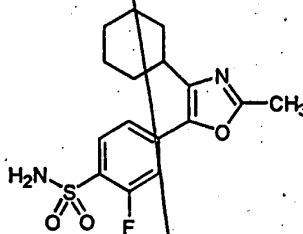
-385-

[1S- ((2R,S)- acetylmercapto- 5- phthalimido]pentanoyl-
L- leucyl)amino- 3- methylbutyl]imidazole.

115. A combination comprising a cyclooxygenase-2 inhibitor, a matrix metalloproteinase inhibitor, and an antineoplastic agent, wherein said antineoplastic agent is selected from the group consisting of anastrozole, calcium carbonate, capecitabine, carboplatin, cisplatin, Cell Pathways CP-461, docetaxel, doxorubicin, etoposide, fluorouracil (5-FU), fluoxymestrine, gemcitabine, goserelin, irinotecan, ketoconazole, letrozol, leucovorin, levamisole, megestrol, mitoxantrone, paclitaxel, raloxifene, retinoic acid, tamoxifen, thiotepa, topotecan, toremifene, vinorelbine, vinblastine, vincristine, selenium (selenomethionine), ursodeoxycholic acid, sulindac sulfone, exemestane and eflornithine (DFMO).

116. The combination of Claim 115 wherein the
20 cyclooxygenase-2 inhibitor is selected from compounds,
and their pharmaceutically acceptable salts thereof, of
the group consisting of:

1)



25 JTE-522, 4-(4-cyclohexyl-2-methyloxazol-5-yl)-
2-fluorobenzenesulfonamide,

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-386-

2)

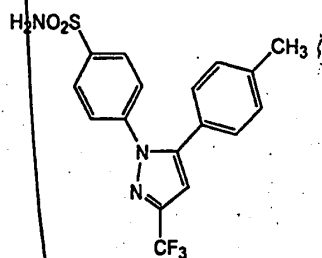
5-chloro-3-(4-(methylsulfonyl)phenyl)-2-(methyl-5-pyridinyl)pyridine,

3)

5

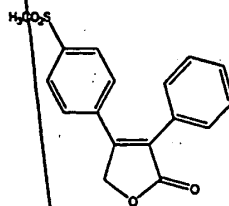
2-(3,5-difluorophenyl)-3-4-(methylsulfonyl)phenyl)-2-cyclopenten-1-one,

4)



4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]-benzenesulfonamide,

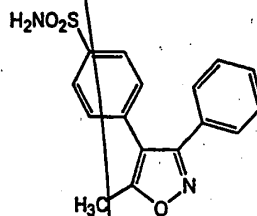
5)



rofecoxib, 4-(4-(methylsulfonyl)phenyl)-3-phenyl-2(5H)-furanone,

6)

15



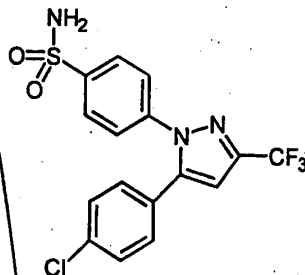
4-(5-methyl-3-phenylisoxazol-4-yl)benzenesulfonamide,

09868000-100501

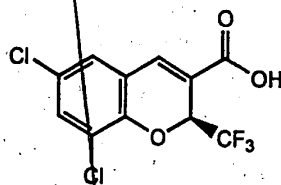
Sup a cont

-387-

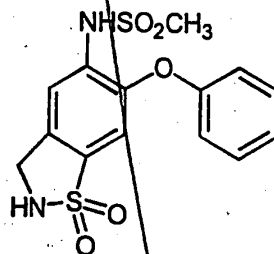
- 7) N-[[4-(5-methyl-3-phenylisoxazol-4-yl)phenyl]sulfonyl]propanamide,
8)



- 5 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazole-1-yl]benzenesulfonamide,
9)

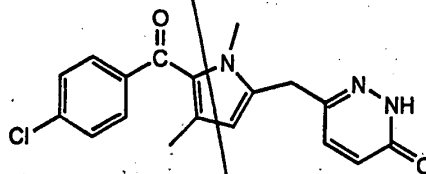


- 10)



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- 11)



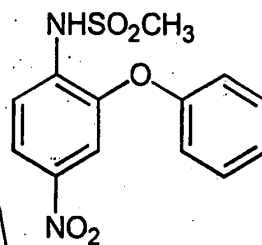
- 6-[[5-(4-chlorobenzoyl)-1,4-dimethyl-1H-pyrrol-2-yl]methyl]-3(2H)-pyridazinone,

0366031001

*Suba
cont*

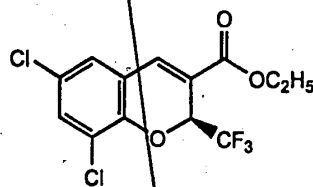
-388-

12)

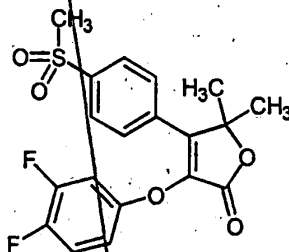


N-(4-nitro-2-phenoxyphenyl)methanesulfonamide,

13)



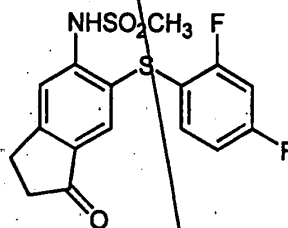
14)



3-(3,4-difluorophenoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-2(5H)-furanone,

10

15)

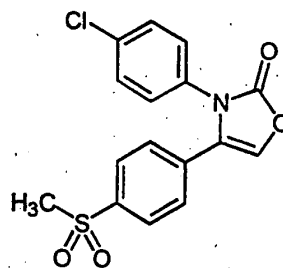


N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,

0936063
105001 29089360
Sub 1
cont

-389-

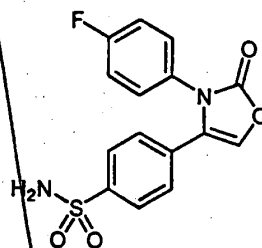
16)



3-(4-chlorophenyl)-4-[4-(methylsulfonyl)phenyl]-2(3H)-oxazolone,

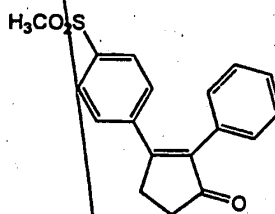
5

17)



4-[3-(4-fluorophenyl)-2,3-dihydro-2-oxo-4-oxazolyl]benzenesulfonamide,

18)



3-[4-(methanesulfonyl)phenyl]-2-phenyl-2-cyclopenten-1-one,

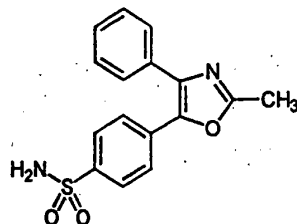
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-390-

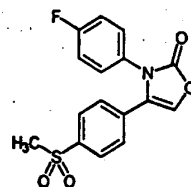
19)



4-(2-methyl-4-phenyl-5-oxazolyl)benzenesulfonamide,

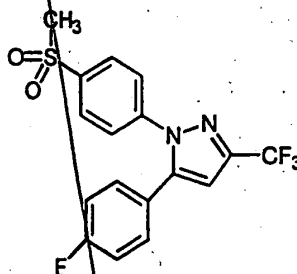
5

20)



3-(4-fluorophenyl)-4-[4-(methylsulfonyl)phenyl]-2(3H)-oxazolone,

21)



10

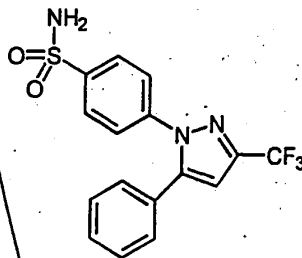
5-(4-fluorophenyl)-1-[4-(methylsulfonyl)phenyl]-3-(trifluoromethyl)-1H-pyrazole,

TOCOTC 9089860

Suba
cont

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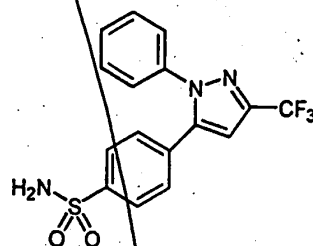
22)



4-[5-phenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide,

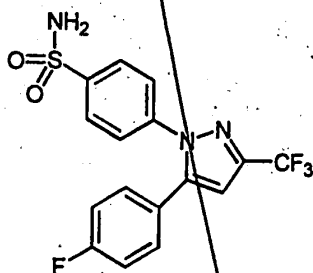
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23)



4-[1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]benzenesulfonamide,

24)



4-[5-(4-fluorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide,

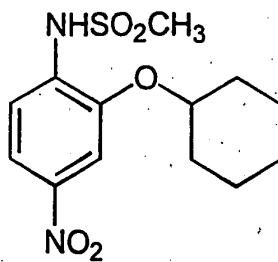
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cont

-392-

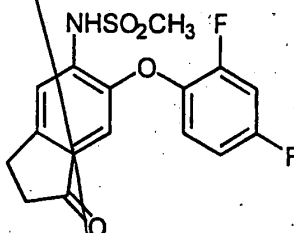
25)



N-[2-(cyclohexyloxy)-4-nitrophenyl]methanesulfonamide,

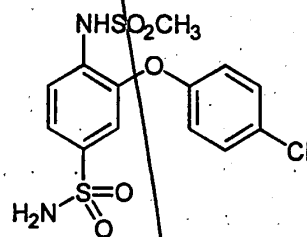
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26)



N-[6-(2,4-difluorophenoxy)-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,

27)

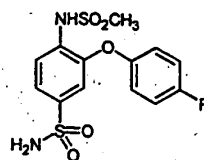


3-(4-chlorophenoxy)-4-
[(methylsulfonyl)amino]benzenesulfonamide,

10

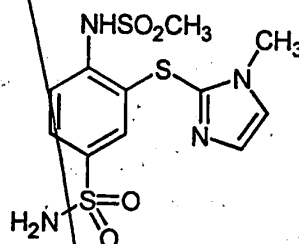
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28)

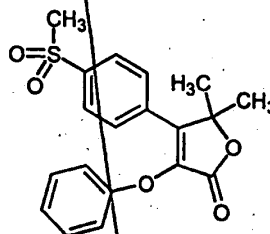


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29)



30)

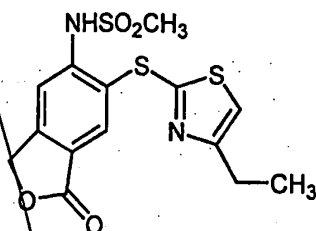


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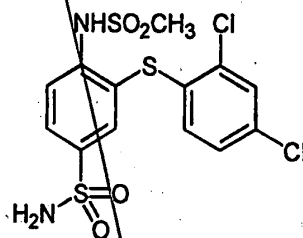
-394-

31)



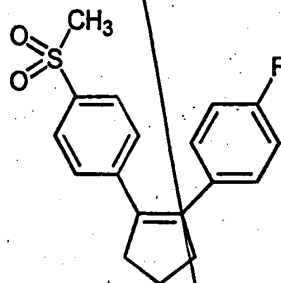
N-[6-[(4-ethyl-2-thiazolyl)thio]-1,3-dihydro-1-oxo-5-isobenzofuranyl]methanesulfonamide,

32)



3-[(2,4-dichlorophenyl)thio]-4-[(methanesulfonyl)amino]benzenesulfonamide,

33)



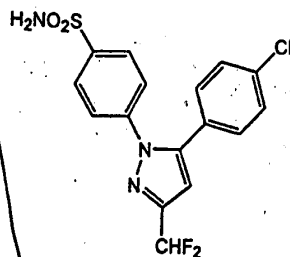
1-fluoro-4-[2-[4-(methanesulfonyl)phenyl]cyclopenten-1-yl]benzene,

09668063100501

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Cont

-395-

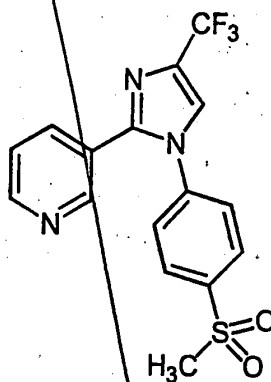
34)



4-[5-(4-chlorophenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide,

5

35)

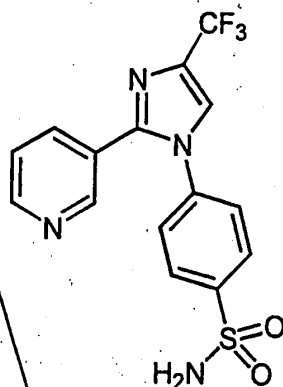


3-[1-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)-1H-imidazol-2-yl]pyridine,

Supp.
Cont

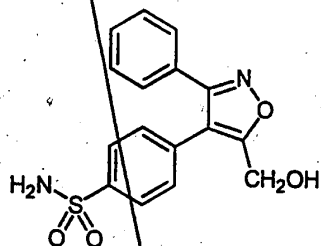
-396-

36)



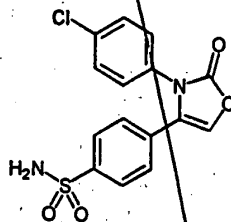
4-[2-(3-pyridinyl)-4-(trifluoromethyl)-1H-imidazol-1-yl]benzenesulfonamide,

37)



4-[5-(hydroxymethyl)-3-phenylisoxazol-4-yl]benzenesulfonamide,

38)



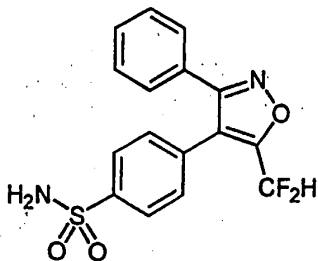
4-[3-(4-chlorophenyl)-2,3-dihydro-2-oxo-4-oxazolyl]benzenesulfonamide,

TO500T-00099960

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Cent

-397-

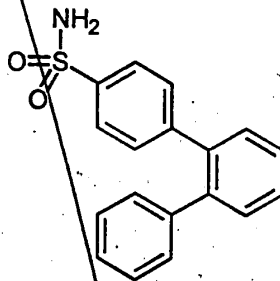
39)



4-[5-(difluoromethyl)-3-phenylisoxazol-4-yl]benzenesulfonamide,

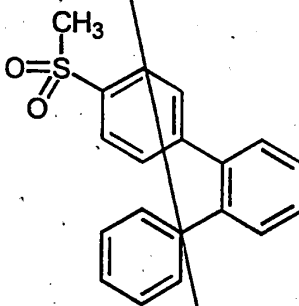
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40)



[1,1':2'',1''-terphenyl]-4-sulfonamide,

41)



4-(methylsulfonyl)-1,1',2'',1''-terphenyl,

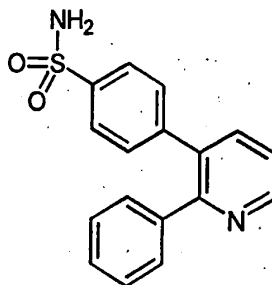
10

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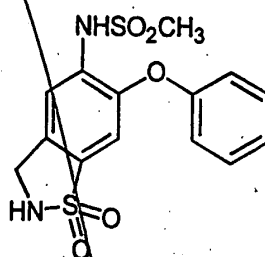
-398-

42)



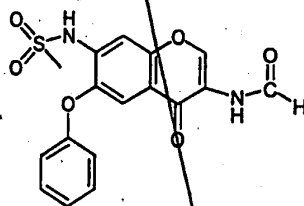
4-(2-phenyl-3-pyridinyl)benzenesulfonamide,

43)



N-(2,3-dihydro-1,1-dioxido-6-phenoxy-1,2-benzisothiazol-5-yl)methanesulfonamide, and

44)



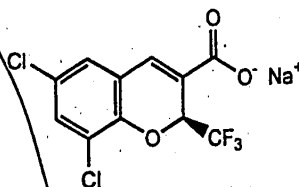
N-[3-(formylamino)-4-oxo-6-phenoxy-4H-1-benzopyran-7-yl]methanesulfonamide,

Sub a!
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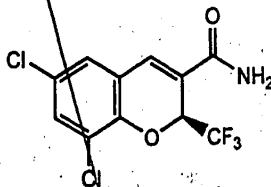
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-399-

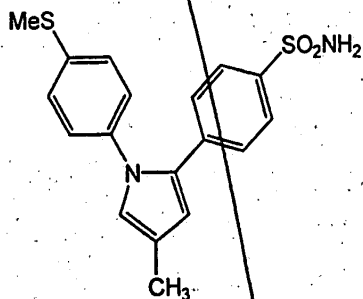
45)



46)

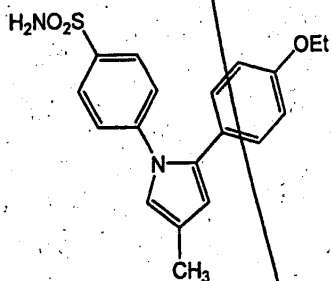


47)



, and

48)

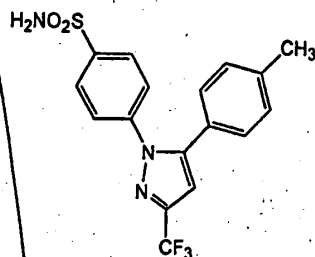


117. The combination of Claim 115 wherein the
 10 cyclooxygenase-2 inhibitor is 5-chloro-3-(4-(methylsulfonyl)phenyl)-2-(methyl-5-pyridinyl)pyridine.

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 5
 Sub 1
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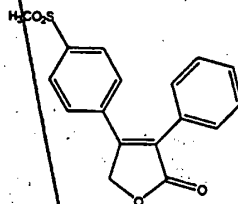
118. The combination of Claim 115 wherein the cyclooxygenase-2 inhibitor is 2-(3,5-difluorophenyl)-3-(4-(methylsulfonyl)phenyl)-2-cyclopenten-1-one.

119. The combination of Claim 115 wherein the
5 cyclooxygenase-2 inhibitor is



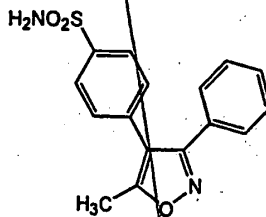
4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]-benzenesulfonamide.

120. The combination of Claim 115 wherein the
10 cyclooxygenase-2 inhibitor is



rofecoxib, 4-(4-(methylsulfonyl)phenyl)-3-phenyl-2(5H)-furanone.

15 121. The combination of Claim 115 wherein the
cyclooxygenase-2 inhibitor is



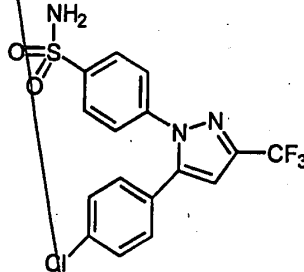
4-(5-methyl-3-phenylisoxazol-4-yl)benzenesulfonamide.

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-401-

122. The combination of Claim 115 wherein the cyclooxygenase-2 inhibitor is N-[[4-(5-methyl-3-phenylisoxazol-4-yl)phenyl]sulfonyl]propanamide.

123. The combination of Claim 115 wherein the
5 cyclooxygenase-2 inhibitor is



4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazole-1-yl]benzenesulfonamide.

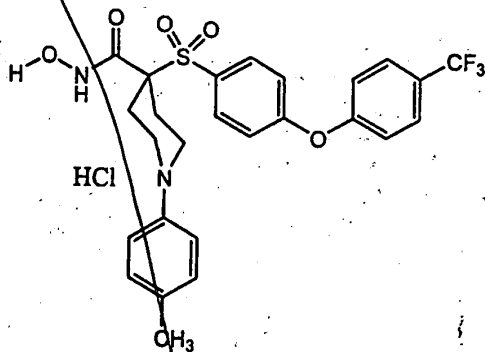
124. The combination of Claim 115 wherein the
10 neoplasia is selected from the group consisting of lung cancer, breast cancer, gastrointestinal cancer, bladder cancer, head and neck cancer and cervical cancer.

125. The combination of Claim 115 wherein the
15 neoplasia is selected from the group consisting of acral lentiginous melanoma, actinic keratoses, adenocarcinoma, adenoid cystic carcinoma, adenomas, adenocarcinoma, adenosquamous carcinoma, astrocytic tumors, Bartholin gland carcinoma, basal cell carcinoma, bronchial gland carcinomas, capillary, carcinoids, carcinoma,
20 carcinosarcoma, cavernous, cholangiocarcinoma, chondrosarcoma, choroid plexus papilloma/carcinoma, clear cell carcinoma, cystadenoma, endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, ependymal, epithelioid,
25 Ewing's sarcoma, fibrolamellar, focal nodular hyperplasia, gastrinoma, germ cell tumors, glioblastoma,

09860063100501
Suba Cont

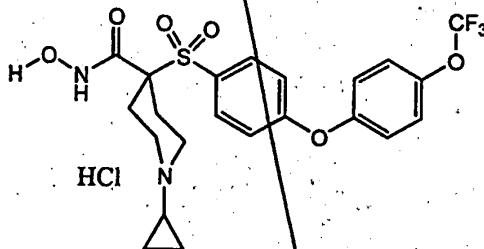
-403-

1)



N-hydroxy-1-(4-methylphenyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

2)



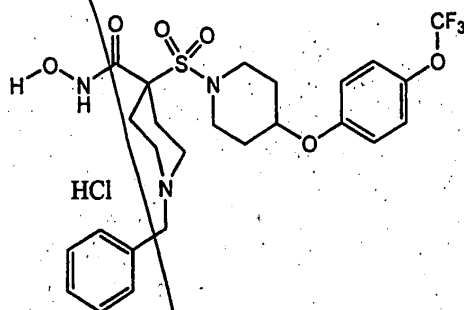
1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

TO500T" C4039860

Sub 1
Cont

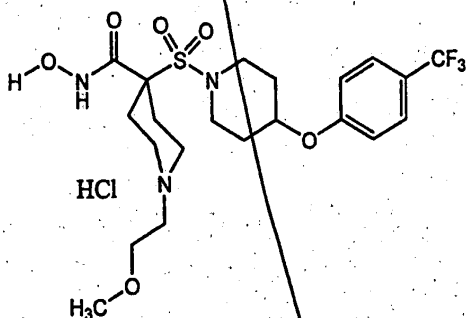
-404-

3)



N-hydroxy-1-(phenylmethyl)-4-[[4-[4-(trifluoromethoxy)phenoxy]-1-piperidinyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

4)



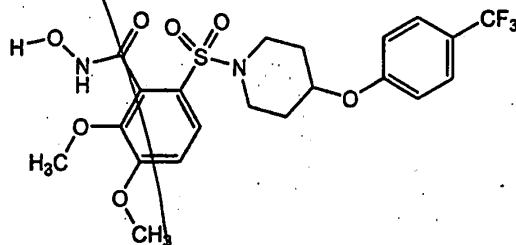
N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

Sub: Cont

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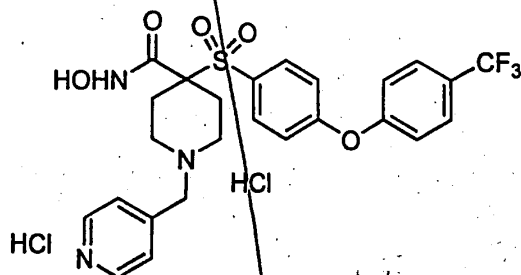
-405-

5)



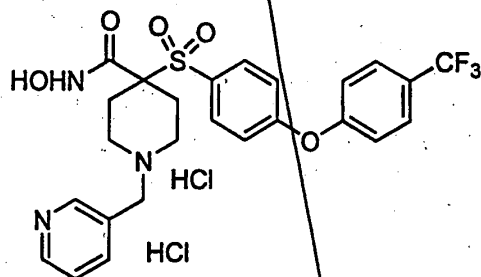
N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide,

6)



N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

7)



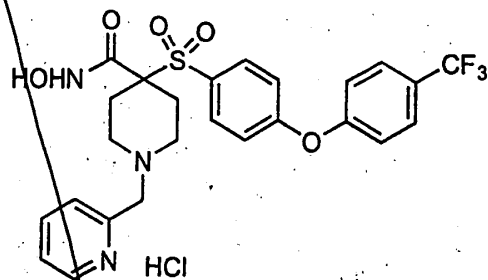
N-hydroxy-1-(3-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

T05001-9089360

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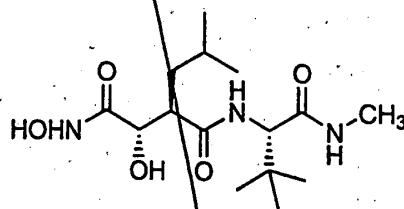
-406-

8)



N-hydroxy-1-(2-pyridinylmethyl)-4-[[4-[(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

9)

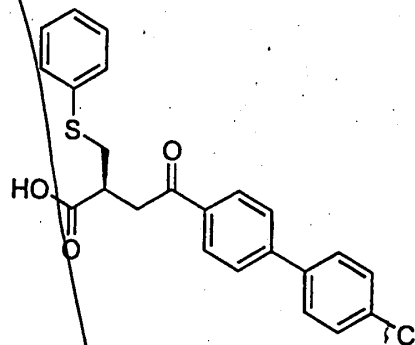


British Biotech BB-2516 (Marimastat), N4-[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1,2-dihydroxy-3 (2-methylpropyl)-, [2S-[N4(R*), 2R*, 3S*]]-,

Suba!
cont

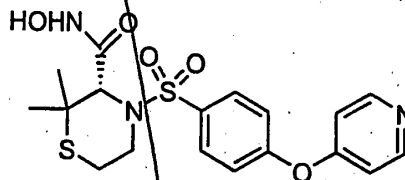
-407-

10)



Bayer Ag Bay-12-9566, 4-[(4'-chloro[1,1'-
iphenyl]- 4-yl)oxy]-2-
[(phenylthio)methyl]butanoic acid,

11)



Agouron Pharmaceuticals AG-3340, N-hydroxy-2,2
dimethyl-4-[[4-(4-
pyridinyloxy)phenyl]sulfonyl] 3-
thiomorpholinecarboxamide,

12) CollaGenex Pharmaceuticals CMT-3 (Metastat),
6-demethyl-6-deoxy-4-
dedimethylaminotetracycline,

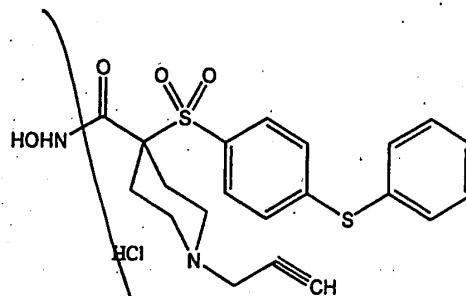
13) Chiroscience D-2163, 2- [1S- ((2R,S)-
acetylmercapto- 5- phthalimidolpentanoyl- L-
leucyl)amino- 3- methylbutyl]imidazole,

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Sub 1
Cont

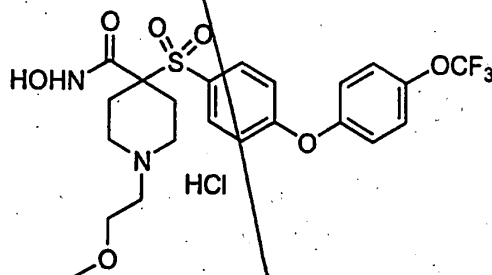
-408-

14)



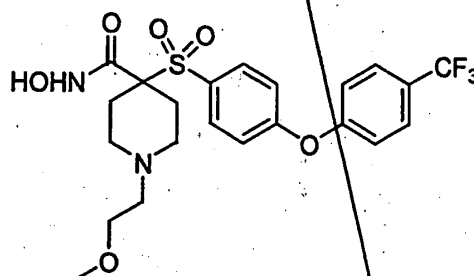
N-hydroxy-4-[[4-(phenylthio)phenyl]sulfonyl]-
1-(2-propynyl)-4-piperidinecarboxamide
monohydrochloride,

15)



N-hydroxy-1-(2-methoxyethyl)-4-[[4-[4-
(trifluoromethoxy) phenoxy]phenyl]sulfonyl]-4-
piperidinecarboxamide monohydrochloride,

16)

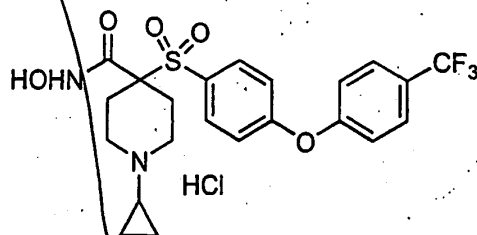


N-hydroxy-1-(2-methoxyethyl)-4-[[4-[4-
(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-
piperidinecarboxamide,

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Cont

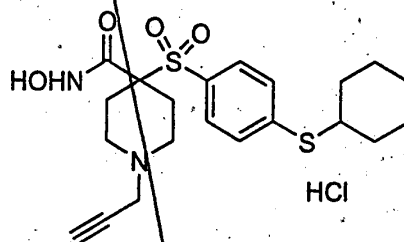
-409-

17)



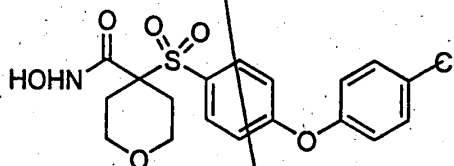
1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

18)



4-[[4-(cyclohexylthio)phenyl]sulfonyl]-N-hydroxy-1-(2-propynyl)-4-piperidinecarboxamide monohydrochloride,

19)



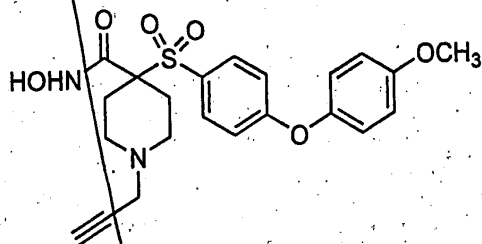
4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-N-hydroxy-2H-pyran-4-carboxamide,

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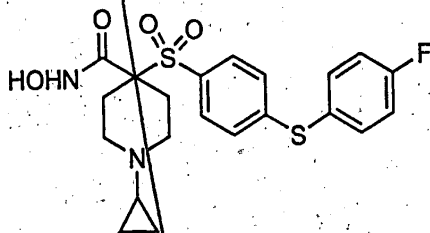
-410-

20)



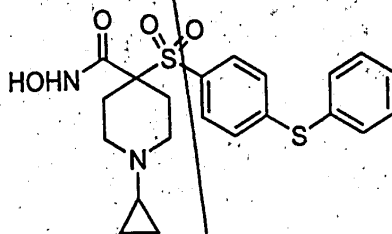
N-hydroxy-4-[[4-(4-methoxyphenoxy)phenyl]sulfonyl]-1-(2-propynyl)-4-piperidinecarboxamide,

21)



1-cyclopropyl-4-[[4-[(4-fluorophenyl)thio]phenyl]sulfonyl]-N-hydroxy-4-piperidinecarboxamide,

22)



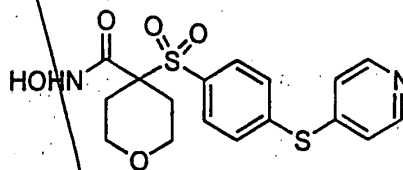
1-cyclopropyl-N-hydroxy-4-[[4-(phenylthio)phenyl]sulfonyl]-4-piperidinecarboxamide,

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Sub a Cont

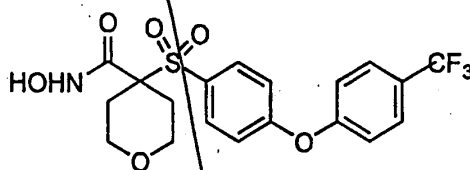
-411-

23)



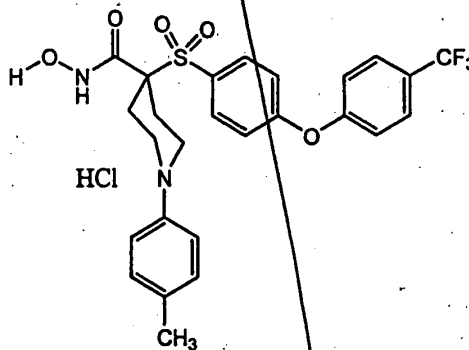
tetrahydro-N-hydroxy-4-[[4-(4-pyridinylthio)phenyl]sulfonyl]-2H-pyran-4-carboxamide, and

24)



tetrahydro-N-hydroxy-4-[[4-(4-(trifluoromethyl)phenoxy)phenyl]sulfonyl]-2H-pyran-4-carboxamide.

127. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



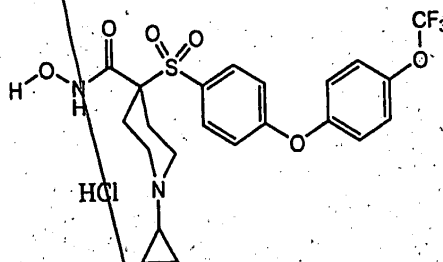
N-hydroxy-1-(4-methylphenyl)-4-[[4-(4-(trifluoromethyl)phenoxy)phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

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Sub a cont

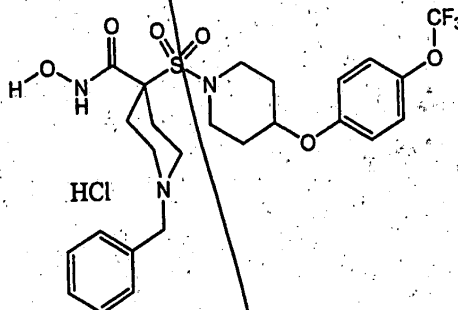
-412-

128. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



1-cyclopropyl-N-hydroxy-4-[[4-[(4-(trifluoromethoxy)phenoxy]phenyl)sulfonyl]-4-piperidinecarboxamide monohydrochloride.

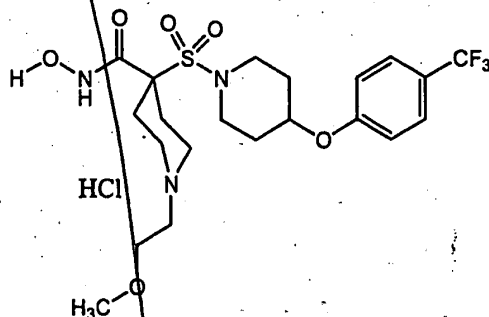
129. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



N-hydroxy-1-(phenylmethyl)-4-[[4-[(4-(trifluoromethoxy)phenoxy]-1-piperidinyl)sulfonyl]-4-piperidinecarboxamide monohydrochloride.

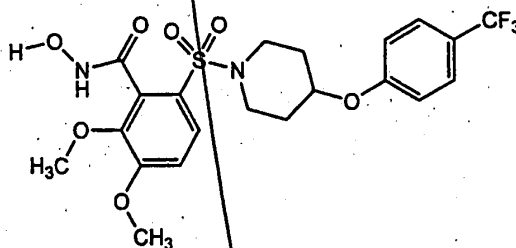
-413-

130. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



5 N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

131. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



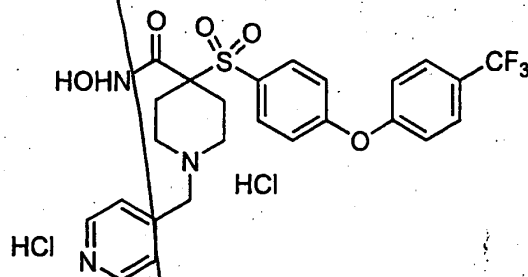
10 N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide.

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cont*

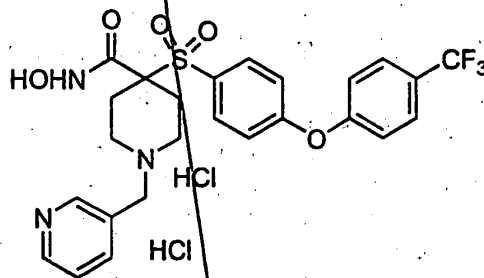
-414-

132. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



5 N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

133. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



10 N-hydroxy-1-(3-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

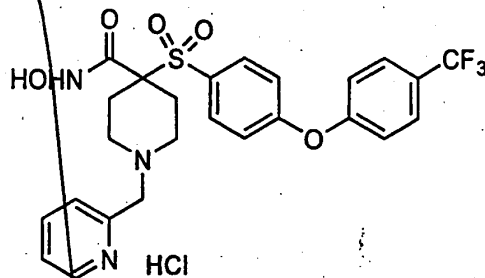
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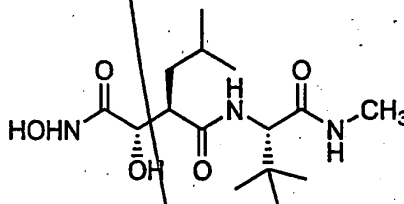
134. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



5

N-hydroxy-1-(2-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

135. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



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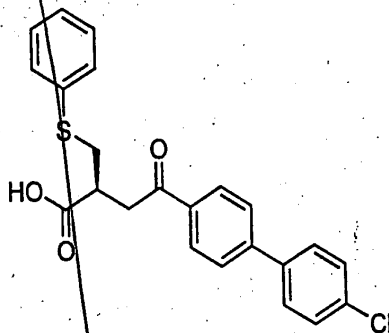
British Biotech BB-2516 (Marimastat), N4-[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1,2-dihydroxy-3 (2-methylpropyl)-, [2S-[N4(R*), 2R*, 3S*]]-).

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cont*

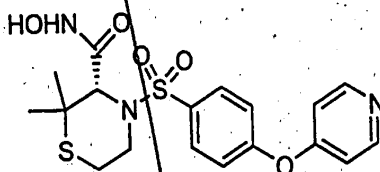
-416-

136. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



5 Bayer Ag Bay-12-9566, 4-[(4'-chloro[1,1'-
iphenyl]-4-yl)oxy]-2-
[(phenylthio)methyl]butanoic acid.

137. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



15 Agouron Pharmaceuticals AG-3340, N-hydroxy-
2,2-dimethyl-4-[[4-(4-
pyridinyloxy)phenyl]sulfonyl]-3-
thiomorpholinecarboxamide.

138. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is CollaGenex
Pharmaceuticals CMT-3 (Metastat), 6-demethyl-6-deoxy-4-
20 dedimethylaminotetracycline.

139. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is Chiroscience D-

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*Sub
a
cont*

-417-

2163, 2- [1S- ([(2R,S)- acetylmercapto- 5-phthalimido]pentanoyl- L- leucyl)amino- 3-methylbutyl]imidazole.

5 140. The method of Claim 1 wherein the antineoplastic agent is anastrozole.

141. The method of Claim 1 wherein the antineoplastic agent is calcium carbonate.

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142. The method of claim 1 wherein the antineoplastic agent is exemestane.

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143. The method of Claim 58 wherein the combination is administered in a sequential manner.

144. The method of Claim 58 wherein the combination is administered in a substantially simultaneous manner.

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145. The method of claim 1 wherein the antineoplastic agent is exemestane.

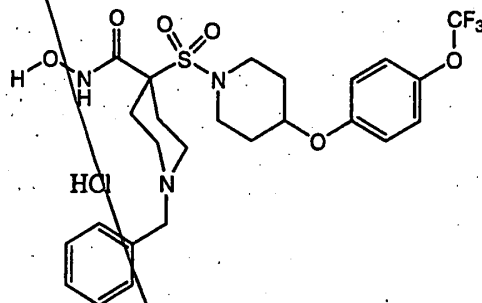
146. A method for treating or preventing a neoplasia disorder in a mammal in need of such treatment or prevention, which method comprises administering to said mammal a therapeutically-effective amount of a combination of a cyclooxygenase-2 inhibitor and a matrix metalloproteinase inhibitor, wherein said matrix metalloproteinase inhibitor is selected from compounds, and their pharmaceutically acceptable salts thereof, of the group consisting of:

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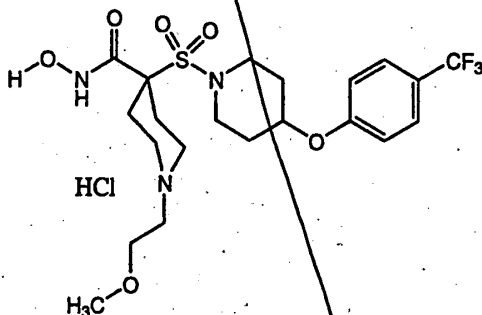
-419-

3)



N-hydroxy-1-(phenylmethyl)-4-[[4-[4-(trifluoromethoxy)phenoxy]-1-piperidinyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

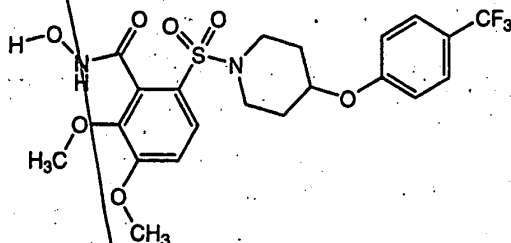
4)



N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

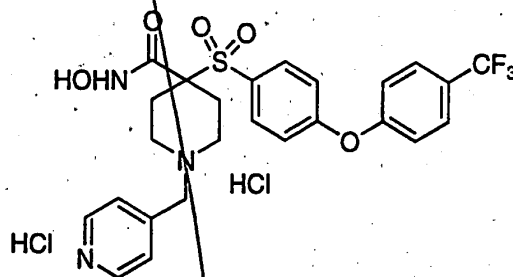
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5)



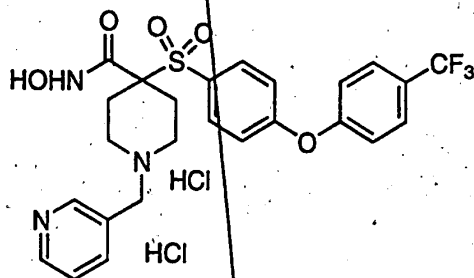
N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide,

6)



N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

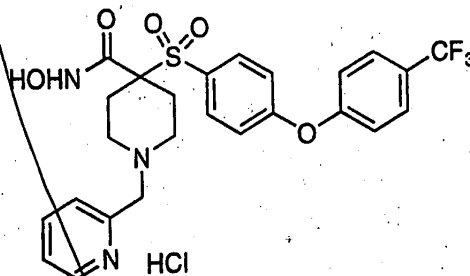
7)



N-hydroxy-1-(3-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

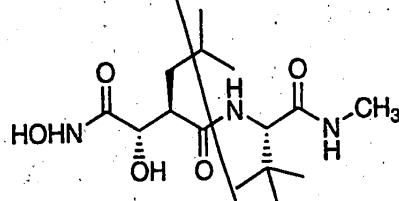
-421-

8)



N-hydroxy-1-(2-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

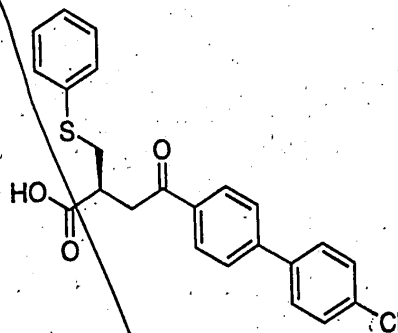
9)



British Biotech BB-2516 (Marimastat), N4-[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1,2-dihydroxy-3 (2-methylpropyl)-, [2S-[N4(R*),2R*,3S*]]-,

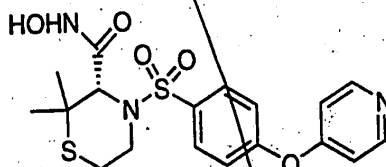
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10)



Bayer Ag Bay-12-9586, 4-[(4'-chloro[1,1'-
biphenyl]-4-yl)oxy]-2-
[(phenylthio)methyl]butanoic acid,

11)



Agouron Pharmaceuticals AG-3340, N-hydroxy-2,2-
dimethyl-4-[[4-(4-
pyridinyloxy)phenyl]sulfonyl]-3-
thiomorpholinecarboxamide,

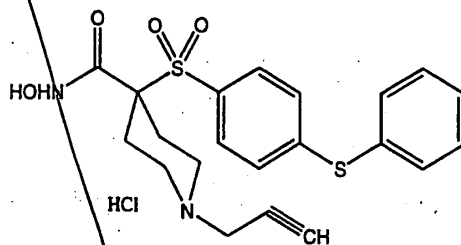
12) CollaGenex Pharmaceuticals CMT-3 (Metastat),
6-demethyl-6-deoxy-4-
dedimethylaminotetracycline,

13) Chiroscience D-2163, 2- [1S- ((2R,S)-
acetylmercapto- 5- phthalimido]pentanoyl- L-
leucyl)amino- 3- methylbutyl]imidazole,

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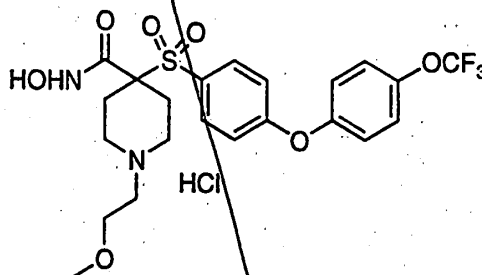
-423-

14)



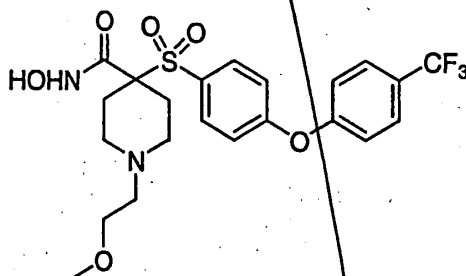
N-hydroxy-4-([4-(phenylthio)phenyl]sulfonyl)-
1-(2-propynyl)-4-piperidinecarboxamide
monohydrochloride,

15)



N-hydroxy-1-(2-methoxyethyl)-4-[[4-[4-
(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-
piperidinecarboxamide monohydrochloride,

16)



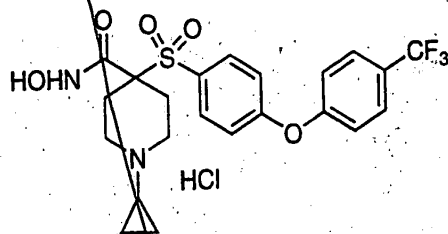
N-hydroxy-1-(2-methoxyethyl)-4-[[4-[4-
(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-
piperidinecarboxamide,

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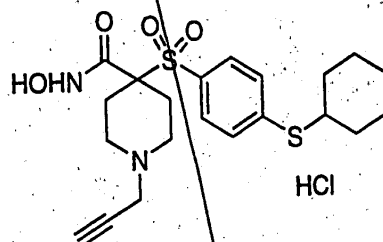
-424-

17)



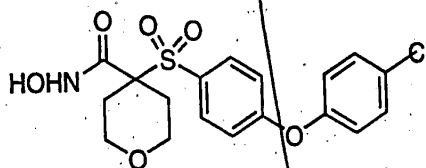
1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

18)



4-[[4-(cyclohexylthio)phenyl]sulfonyl]-N-hydroxy-1-(2-propynyl)-4-piperidinecarboxamide monohydrochloride,

19)

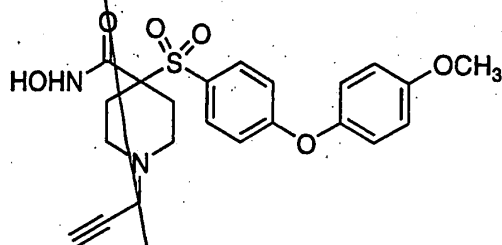


4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-N-hydroxy-2H-pyran-4-carboxamide,

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Cont

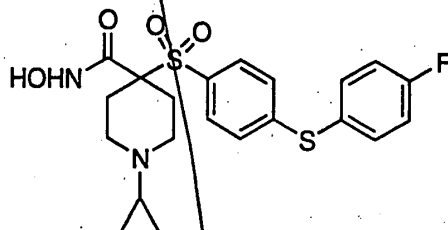
-425-

20)



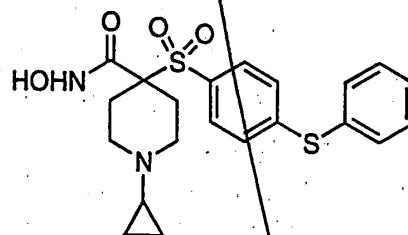
N-hydroxy-4-[[4-(4-methoxyphenoxy)phenyl)sulfonyl]-1-(2-propynyl)-4-piperidinecarboxamide,

21)



1-cyclopropyl-4-[[4-[(4-fluorophenyl)thio]phenyl]sulfonyl]-N-hydroxy-4-piperidinecarboxamide,

22)



1-cyclopropyl-N-hydroxy-4-[[4-(phenylthio)phenyl]sulfonyl]-4-piperidinecarboxamide,

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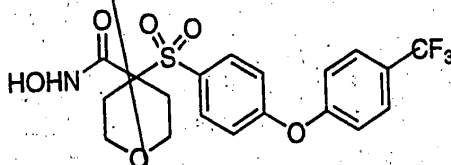
10

15

O=C(O)C1(C(=O)S(=O)(=O)c2ccc(Sc3ccccc3)cc2)OCCO1

tetrahydro-N-hydroxy-4-[[4-(4-pyridinylthio)phenyl]sulfonyl]-2H-pyran-4-carboxamide, and

24)



tetrahydro-N-hydroxy-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-2H-pyran-4-carboxamide.

147. The method of Claim 146 comprising administering to said mammal a therapeutically-effective amount of a combination of an cyclooxygenase-2 inhibitor, a matrix metalloproteinase inhibitor, and an antineoplastic agent, wherein the antineoplastic agent is selected from the group consisting of anastrozole, calcium carbonate, capecitabine, carboplatin, cisplatin, Cell Pathways CP-461, docetaxel, doxorubicin, etoposide, fluorouracil (5-FU), fluoxymestriene, gemcitabine, goserelin, irinotecan, ketoconazole, letrozol, leucovorin, levamisole, megestrol, mitoxantrone, paclitaxel, raloxifene, retinoic acid, tamoxifen, thiotepa, topotecan, toremifene, vinorelbine, vinblastine, vincristine, selenium (selenomethionine),

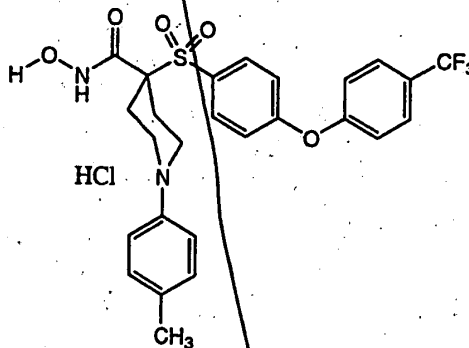
-427-

ursodeoxycholic acid, sulindac sulfone and eflornithine (DFMO).

148. The method of Claim 146 comprising
5 administering to said mammal a therapeutically-effective amount of a combination of radiation, a cyclooxygenase-2 inhibitor and a matrix metalloproteinase inhibitor.

149. A combination comprising a cyclooxygenase-2
10 inhibitor and a matrix metalloproteinase inhibitor, wherein said matrix metalloproteinase inhibitor is selected from compounds, and their pharmaceutically acceptable salts thereof, of the group consisting of:

1)

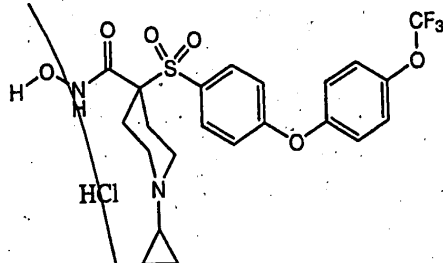


15 N-hydroxy-1-(4-methylphenyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

20

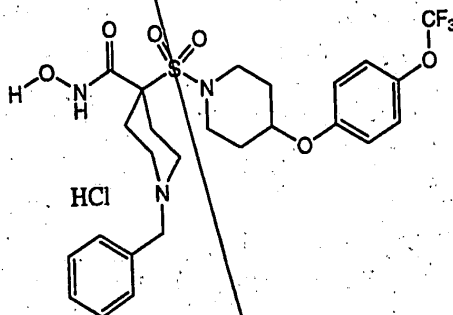
2)

-428-



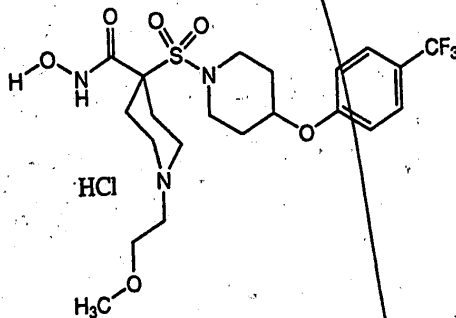
1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

3)



N-hydroxy-1-(phenylmethyl)-4-[[4-[4-(trifluoromethoxy)phenoxy]-1-piperidinyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

4)

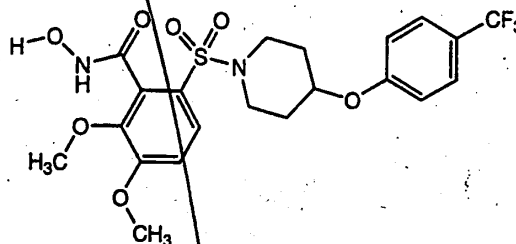


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-429-

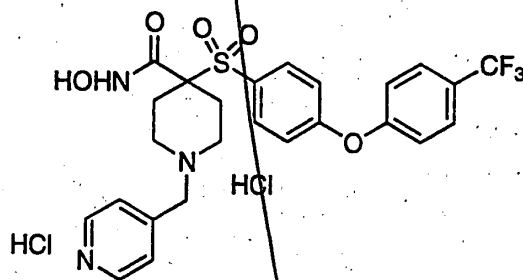
N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

5)



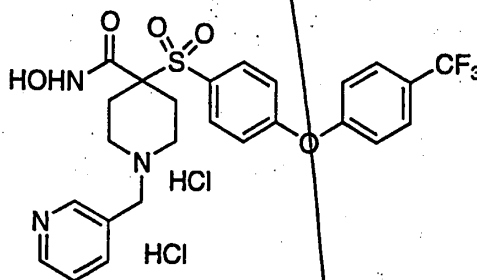
N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide,

6)



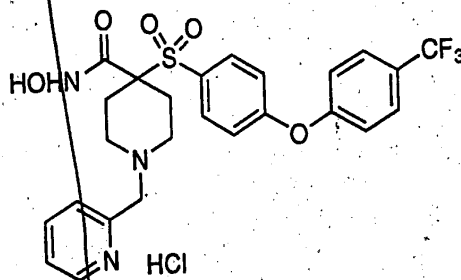
N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

7)



5

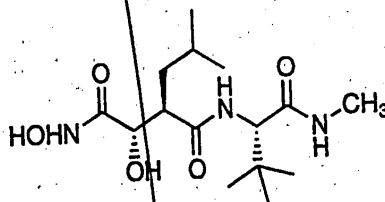
8)



N-hydroxy-1-(2-pyridinylmethyl)-4-[[4-(4-(trifluoromethyl)phenoxy)phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

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9)

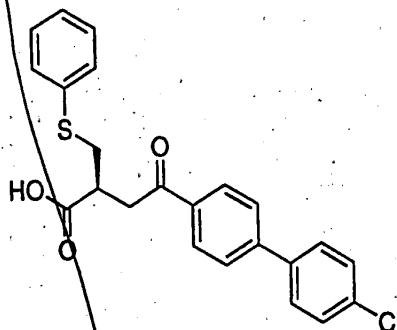


British Biotech BB-2516 (Marimastat), N4-[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1,2-dihydroxy-3 (2-methylpropyl)-, [2S-[N4(R*), 2R*, 3S*]]-),

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10)

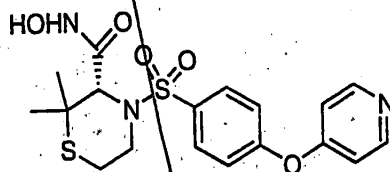
-431-



Bayer Ag Bay-12-9566, 4-[(4'-chloro[1,1'-
iphenyl]-4-yl)oxy]-2-
[(phenylthio)methyl]butanoic acid,

5

11)



Agouron Pharmaceuticals AG-3340, N-hydroxy-2,2
dimethyl-4-[[4-(4-
pyridinyloxy)phenyl]sulfonyl] 3-
thiomorpholinecarboxamide,

10

12) CollaGenex Pharmaceuticals CMT-3 (Metastat),
6-demethyl-6-deoxy-4-
dedimethylaminotetracycline,

15

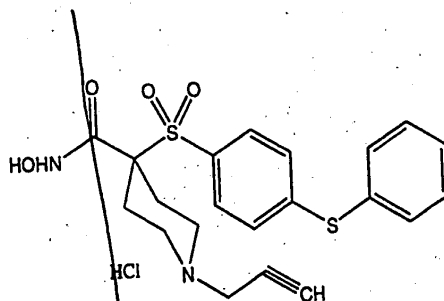
13) Chiroscience D-2163, 2- [1S- ([(2R,S)-
acetylmercapto- 5- phthalimido]pentanoyl- L-
leucyl)amino- 3- methylbutyl]imidazole,

09868763100501

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-432-

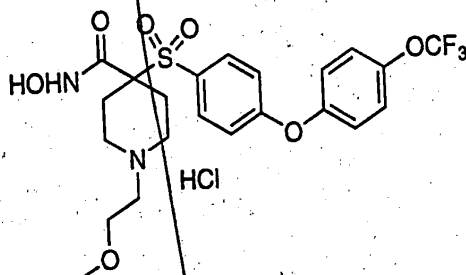
14)



N-hydroxy-4-[[4-(phenylthio)phenyl]sulfonyl]-
1-(2-propynyl)-4-piperidinecarboxamide
monohydrochloride,

5

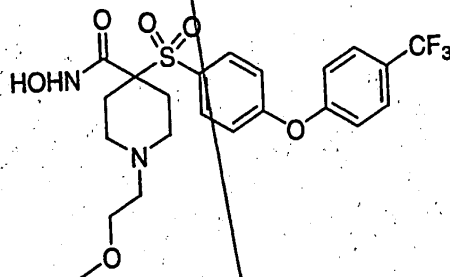
15)



N-hydroxy-1-(2-methoxyethyl)-4-[[4-[[4-
(trifluoromethoxy) phenoxy]phenyl]sulfonyl]-4-
piperidinecarboxamide monohydrochloride,

10

16)



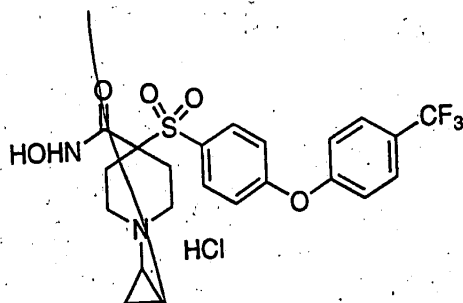
N-hydroxy-1-(2-methoxyethyl)-4-[[4-[[4-
(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-
piperidinecarboxamide,

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09860063-100504
T050079008860
Sub a
cont

-433-

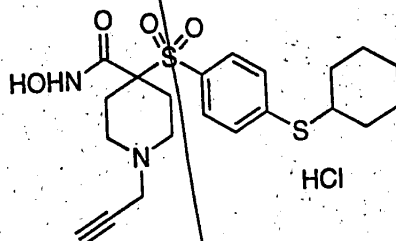
17)



1-cyclopropyl-N-hydroxy-4-[[4-[(4-(trifluoromethyl)phenoxy)phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

5

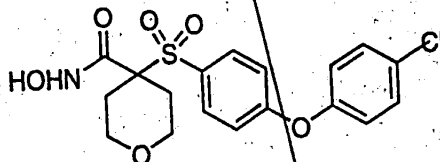
18)



4-[[4-(cyclohexylthio)phenyl]sulfonyl]-N-hydroxy-1-(2-propynyl)-4-piperidinecarboxamide monohydrochloride,

10

19)



4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-N-hydroxy-2H-pyran-4-carboxamide,

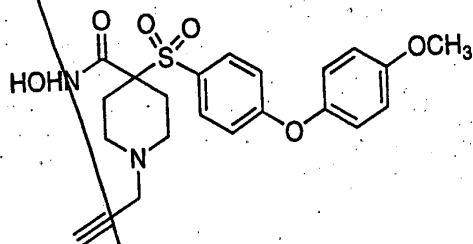
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cont

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-434-

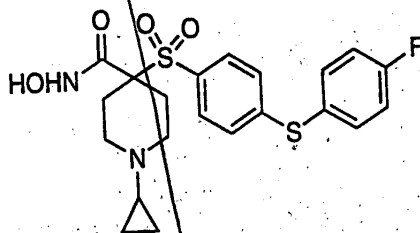
20)



N-hydroxy-4-[[4-(4-methoxyphenoxy)phenyl]sulfonyl]-1-(2-propynyl)-4-piperidinecarboxamide,

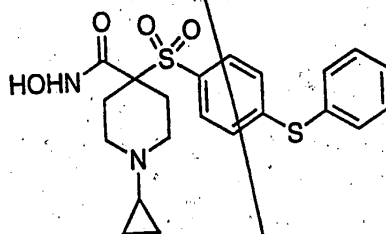
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21)



1-cyclopropyl-4-[[4-[(4-fluorophenyl)thio]phenyl]sulfonyl]-N-hydroxy-4-piperidinecarboxamide,

22)



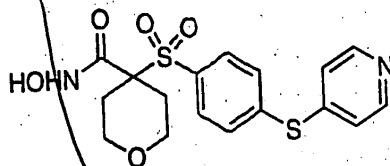
1-cyclopropyl-N-hydroxy-4-[[4-(phenylthio)phenyl]sulfonyl]-4-piperidinecarboxamide,

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Sub 1
Cont

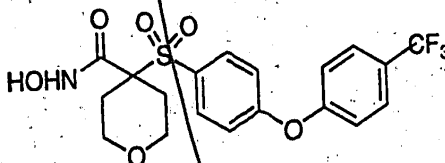
-435-

23)



tetrahydro-N-hydroxy-4-[[4-(4-pyridinylthio)phenyl]sulfonyl]-2H-pyran-4-carboxamide, and

24)



tetrahydro-N-hydroxy-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-2H-pyran-4-carboxamide.

Sub 1
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